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Note

A convenient route to alkyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosides

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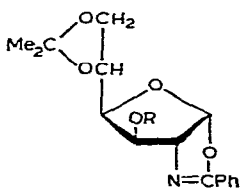
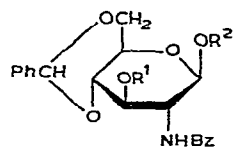
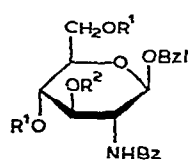
We observed in previous work[1] that the highly crystalline benzylidene derivative **4** separated from the reaction mixture when the phenyloxazoline **1** was kept in acidified benzyl alcohol (containing 0.2% of benzaldehyde as an impurity). The addition of an excess of benzaldehyde to the reaction mixture allowed[1] the preparation of **4** in high yield. This serendipitous observation prompted us to investigate the general nature of the reaction and we now show that other alkyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosides (**5**, **7**, **9**, **11**, and **13**) can be prepared in good yields by this procedure using the phenyloxazolines (**1**–**3**) and the appropriate alcohol. The



1 R = Bzl
2 R = $-CH_2CH{=}CH_2$
3 R = H



4 $R^1 = R^2 =$ Bzl
5 R^1 = Bzl, $R^2 = -CH_2CH{=}CH_2$
6 R^1 = Bzl, $R^2 = -CH{=}CHMe$
7 $R^1 = -CH_2CH{=}CH_2$, R^2 = Bzl
8 $R^1 = -CH{=}CHMe$, R^2 = Bzl
9 R^1 = H, $R^2 = -CH_2CH{=}CH_2$
10 R^1 = Ac, $R^2 = -CH_2CH{=}CH_2$
11 R^1 = H, R^2 = Bzl
12 R^1 = Ac, R^2 = Bzl
13 R^1 = H, $R^2 = -CH_2C(Me){=}CH_2$
14 R^1 = Ac, $R^2 = -CH_2C(Me){=}CH_2$
15 R^1 = Bzl, R^2 = H



16 R^1 = H, $R^2 = -CH_2CH{=}CH_2$
17 R^1 = Ac, $R^2 = -CH_2CH{=}CH_2$

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alcohols **9**, **11**, and **13** were characterised as the acetates, since the free alcohols crystallised from alcoholic solvents with alcohol of crystallisation.

The preparation entails a sequence of four reactions: (*a*) opening of the oxazoline ring to give a β-glucofuranoside, (*b*) deacetonation, (*c*) conversion of a β-furanoside into a β-pyranoside, and (*d*) formation of the benzylidene derivative. The first three reactions were studied in detail by Zervas and his co-workers[2] after the discovery of compound **3**, and subsequently by other workers (see ref. 1), and the ease with which the benzylidene derivatives separate from the reaction mixture (which is incompatible with their existence) is presumably a result of their high degree of crystallinity.

When **11** was prepared by this procedure, the reaction mixture was gelatinous and acetone was added to aid filtration of the product. Compound **11** was more conveniently prepared from the benzyl glycoside **7** by isomerisation[3] of the allyl group and removal[4] of the resulting prop-1-enyl group with mercuric chloride–mercuric oxide.

We have previously[1] developed a method for the hydrolysis of the benzylidene group from **4**, by treatment with dilute hydrochloric acid in dimethyl sulphoxide, and this method was used for the hydrolysis of the benzylidene group from **7** to give the diol **16**, which was characterised as the acetate **17**. The removal of the benzylidene group from these compounds liberates hydroxyl groups which can be further substituted to give other useful intermediates (see ref. 1) and, since the benzamido group can be transformed into acetamido or other acylamino groups (see following paper[5]), these readily prepared intermediates should be useful for synthetic work in the amino-sugar series.

The allyl glycoside **5** was converted into the prop-1-enyl glycoside **6** by the action of potassium *tert*-butoxide in dimethyl sulphoxide[3], and hydrolysis[4] of the prop-1-enyl group with mercuric chloride–mercuric oxide gave the free sugar **15**. Both **6** and **15** have been converted into phenyloxazolines (see following paper[6]).

EXPERIMENTAL

Solvents were evaporated under reduced pressure. Optical rotations were measured with a Bendix automatic polarimeter.

General conditions for the preparation of the alkyl 2-benzamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosides. — A solution of the phenyloxazoline (5 mmol) in the alcohol (50 mL) containing benzaldehyde (2.5 mL) and *p*-toluenesulphonic acid monohydrate (1 g) was kept at 20°. Crystallisation of the product usually started within 1.5 h; after 12 h, the product was filtered off, and washed with a little of the alcohol and then with light petroleum (b.p. 40–60°). The product was then stirred with dilute, aqueous ammonia (to neutralise traces of *p*-toluenesulphonic acid) before filtering and drying.

Allyl 2-benzamido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**5**). — The reaction of the benzyl ether **1**[4,7] in allyl alcohol gave **5** (75%), m.p.

265–270° (dec.) (from $HCONMe_2$), $[\alpha]_D^{28}$ −19° (*c* 0.4, *N*,*N*-dimethylformamide).

Anal. Calc. for $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79. Found: C, 71.72; H, 6.14; N, 2.79.

Benzyl 3-O-allyl-2-benzamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**7**). — The reaction of the allyl ether **2**[4] in benzyl alcohol gave **7** (80%), m.p. 305° (dec.) (from $HCONMe_2$), $[\alpha]_D^{28}$ −55° (*c* 0.3, *N*,*N*-dimethylformamide).

Anal. Calc. for $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79. Found: C, 71.49; H, 6.18; N, 2.84.

Allyl 3-O-acetyl-2-benzamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**10**). — Allyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**9**, 80%) was prepared from the alcohol **3** by the reaction in allyl alcohol and characterised as the acetate **10** (prepared by the action of acetic anhydride–pyridine), m.p. 294–303° (dec.) (from ethyl acetate–ethanol, 2:1), $[\alpha]_D^{30}$ −72° (*c* 1, pyridine).

Anal. Calc. for $C_{25}H_{27}NO_7$: C, 66.21; H, 6.00; N, 3.09. Found: C, 66.38; H, 6.21; N, 3.14.

Benzyl 3-O-acetyl-2-benzamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**12**). — (*a*) Benzyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**11**) was prepared from the alcohol **3** in benzyl alcohol by the general procdure, but the reaction mixture was gelatinous at the end of the reaction. Acetone (a volume equal to that of the benzyl alcohol) was therefore added before filtration, and compound **11** (70%) was characterised as the acetate **12**, m.p. 305–315° (dec.) (from ethyl acetate–ethanol, 2:1), $[\alpha]_D^{32}$ −86° (*c* 1, pyridine); lit.[8] m.p. 312°, $[\alpha]_D^{25}$ −85° (pyridine).

Anal. Calc. for $C_{29}H_{29}NO_7$: C, 69.17; H, 5.81; N, 2.78. Found: C, 68.84; H, 5.94; N, 2.88.

(*b*) Compound **7** (1.3 g) was added to a solution of potassium *tert*-butoxide (1 g) in dry dimethyl sulphoxide (50 mL), and the solution was kept at 50° for 3 h. Water (100 mL) was added, and the precipitated prop-1-enyl ether **8** (1.2 g) was collected by filtration and washed with water. Compound **8** was stirred with a mixture of acetone–water (10:1, 25 mL), mercuric chloride (500 mg), and mercuric oxide (500 mg) for 12 h at 20°. Water (50 mL) was then added and the mixture filtered. The solid residue was washed with water, saturated, aqueous potassium iodide (to dissolve the mercuric oxide), and water, and dried. The crude product was acetylated to give **12** (785 mg), m.p. and mixture m.p. [with material prepared in (*a*)] 305–315° (dec.) (from acetonitrile), $[\alpha]_D^{30}$ −87° (*c* 1, pyridine).

2-Methylallyl 3-O-acetyl-2-benzamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**14**). — 2-Methylallyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**13**, 50%) was prepared by the general procedure from the alcohol **3** and 2-methylallyl alcohol, and was characterised as the acetate **14**, m.p. and mixture m.p. (with material prepared previously[9]) 288–295° (dec.) (from ethyl acetate–ethanol, 2:1), $[\alpha]_D^{32}$ −70° (*c* 1, pyridine), $[\alpha]_D^{28}$ −23.5° (*c* 0.5, chloroform); lit.[9] m.p. 288.5–294°, $[\alpha]_D^{22}$ −30.8° (chloroform).

Benzyl 4,6-di-O-acetyl-3-O-allyl-2-benzamido-2-deoxy-β-D-glucopyranoside (**17**).

— The benzyl glycoside **7** was hydrolysed with dilute hydrochloric acid in dimethyl sulphoxide, as described[1] for the hydrolysis of **4**, to give the diol **16** (70%), which was characterised as the acetate **17**, m.p. 206–208° (from ethanol), $[\alpha]_D^{26}$ −12° (*c* 0.5, chloroform).

Anal. Calc. for $C_{27}H_{31}NO_8$: C, 65.18; H, 6.28; N, 2.82. Found: C, 64.99; H, 6.28; N, 2.88.

Prop-1-enyl 2-benzamido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**6**). — Compound **5** (5 g) was treated with potassium *tert*-butoxide (1 g) in dry dimethyl sulphoxide (50 mL) at 50° for 3 h and the product was isolated by dilution with water, filtration, and washing with water. The crude, dry product (4.7 g) was recrystallised from acetonitrile to give **6**, m.p. 282–285° (dec.), $[\alpha]_D^{21}$ −35° (*c* 0.5, *N*,*N*-dimethylformamide), ν_{max} 1670 (-O-CH=CH) and 1640 cm^{-1} (-NHCO-).

Anal. Calc. for $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79. Found: C, 71.81; H, 6.12; N, 2.67.

2-Benzamido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-D-glucopyranose (**15**). — The prop-1-enyl glycoside **6** was hydrolysed with mercuric chloride–mercuric oxide, as described above for the hydrolysis of compound **8**. The crude product was recrystallised from acetonitrile to give **15**, m.p. 236–242° (dec.), $[\alpha]_D^{21}$ +38° (*c* 0.5, *N*,*N*-dimethylformamide).

Anal. Calc. for $C_{27}H_{27}NO_6$: C, 70.26; H, 5.90; N, 3.04. Found: C, 70.00; H, 5.95; N, 2.95.

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