Carbohydrate Research, 102 (1982) 308–311
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

Methyl 2-*O*-acetyl-4-*O*-benzoyl-α-D-*ribo*-hexopyranosid-3-ulose

Vernon G. S. Box*, Lynda L. Box, and Earle V. E. Roberts
Chemistry Department, University of the West Indies, Kingston 7, Jamaica (West Indies)

(Received April 30th, 1981; accepted for publication in revised form, July 15th, 1981)

The *C*-acylation of keto-sugars has been explored but appears to be an unfavourable synthetic route to branched-chain sugars[1]. This work describes another attempt at *C*-acylation of an enolate derived from a keto-sugar, and an attempted photo-Fries rearrangement of an enol ester[2]. The photochemical route to *C*-acylation, though unsuccessful, furnished us with a protected sugar of synthetic value.

In the course of preparing methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*arabino*-hexopyranosid-2-ulose (**1**) from methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) by oxidation with dimethyl sulfoxide–acetic anhydride[3], we observed that prolonged reaction-times resulted in the slow formation of materials other than **1**. The ketone **1**, on prolonged exposure to the oxidant, was also slowly converted into the same mixture of products. As the reaction seemed to proceed via the enol or enolate of **1**, we were lured by the prospect of achieving *C*-acylation of **1**. Exploration of the reaction showed that the yield of the products and the rate of the transformation could be optimised by catalysing the process with either sodium acetate or triethylamine. This finding indicated that the enolate of **1** was indeed the reactive intermediate.

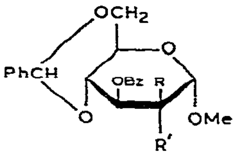
Unfortunately, the major product of the reaction proved to be an enol ester[4], whose structure was shown by its i.r. and n.m.r. spectra to be methyl 2-*O*-acetyl-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*erythro*-hex-2-enopyranoside (**3**). Interestingly, H-1 did not show appreciable long-range coupling[5] to H-4 in the n.m.r. spectrum of **3**.

Reduction of **3** with sodium borohydride in methanol gave methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, which was characterised as its diacetate, thus providing unequivocal evidence for the enol ester structure given to **3**.

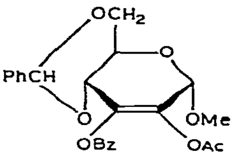
Because **3** was readily available and seemed an ideal substrate for a photo-Fries rearrangement[2], it was irradiated by sunlight for 65 h and so was transformed *cleanly*, in 83% yield, into the unexpected product **4** and benzaldehyde. The enol ester **3** is quite stable and so too are its neutral solutions. Exposure of **3** to dilute methanolic hydrogen chloride resulted in its rapid fragmentation, *without* the pro-

---

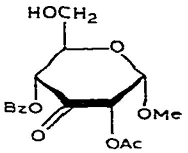
*To whom all correspondence should be addressed.



1 $R = R' = O$
2 $R = H, R' = OH$



3

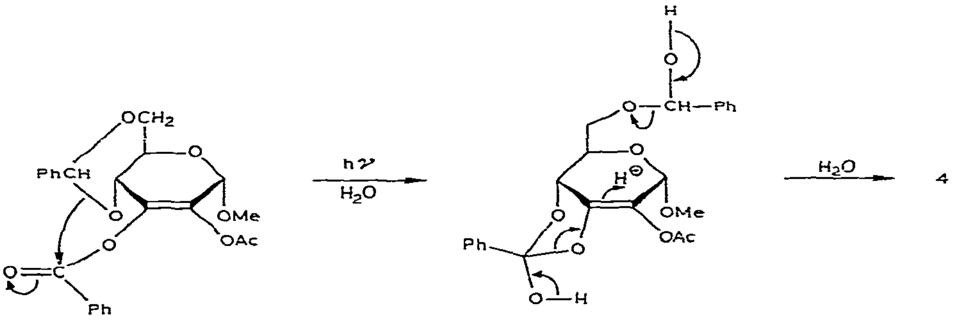


4

duction of **4**. The ketone **4** was therefore genuinely the product of a photochemical reaction. The structure of **4** was determined to be methyl 2-*O*-acetyl-4-*O*-benzoyl-α-D-*ribo*-hexopyranosid-3-ulose from its i.r. and n.m.r. spectra.

Remarkably, every proton's resonance was observed and so the n.m.r. spectrum defined the structure and configuration of **4** unequivocally[6].

Because benzaldehyde was the co-fragment formed in the production of **4**, the reaction did not involve initial photo-oxidation at the benzylic carbon atom, as benzoic acid would then have been the co-fragment. No benzoic acid was formed in the reaction. The course of the reaction and the yield of **4** were not affected by performing the reaction under nitrogen. It seems unlikely that the transformation is a free-radical reaction and so we have suggested an ionic mechanism for the reaction, as outlined in Scheme 1.



Scheme 1

The remarkable specificity of this photochemical transformation thus has made compound **4** available in 52% overall yield from the very readily obtainable compound **1**.

This type of photochemical reaction might be exploitable as a means of preparing such compounds as **4** but having ester groups other than benzoate at C-4.

EXPERIMENTAL

General methods. — Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer 735B spectrophotometer and are for chloroform solutions. N.m.r. spectra were recorded with a Jeol JNM-PMX60 spectrometer and are for solutions in $CDCl_3$. The chemical shifts were measured relative to tetramethylsilane as the internal standard. All rotations were measured with solutions in chloroform. Thin layer and preparative t.l.c. used silica gel $PF_{254+366}$ (Merck); chromatograms were observed under a Hanovia Chromatolite u.v. lamp, and components made visible by exposure to iodine vapour. The light petroleum used as a solvent or eluant had a boiling range 60–80°. Solutions were dried with sodium sulphate and evaporated with a rotary evaporator (Büchi).

*Methyl 2-*O*-acetyl-3-*O*-benzoyl-4,6-*O*-benzylidene-α-*D-erythro*-hex-2-enopyranoside* (3). — *Method A*. Methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*arabino*-hexopyranosid-2-ulose (2, 0.5063 g, 1.3 mmol) was dissolved in dimethyl sulfoxide (8 mL) and acetic anhydride (5 mL) was added. Anhydrous sodium acetate (2.0192 g, 24.6 mmol) was added and the mixture stirred for 120 h at room temperature. The mixture was poured into cold, saturated sodium carbonate solution (100 mL) and this was extracted with ethyl acetate (4 × 50 mL). The organic solution was washed with brine (1 × 100 mL), dried, and evaporated to a brown gum (0.8384 g). Separation of the components of the mixture by preparative t.l.c. (3:1 light petroleum–ethyl acetate) yielded white crystals of 3 (0.2376 g, 69% based on reacted starting material) and unreacted starting material (0.1959 g). Recrystallisation of 3 from light petroleum yielded white crystals, m.p. 127–128°, $[\alpha]_D^{28}$ +30° (*c*, 1.01); ν_{max} 1742 and 1780 cm^{-1} and signals in the n.m.r. spectrum at δ 2.10 and 3.47 (each 3 H, s, $COCH_3$ and O-CH_3), 4.83 (1 H, m, H-5), 5.13 and 5.50 (each 1 H, s, H-1 and C*H*-Ph respectively), 7.33 (8 H, m), and 8.00 (2 H, m).

Anal. Calc. for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20; O, 30.02. Found: C, 64.19; H, 5.26; O, 30.60.

Method B. Compound **2** (0.2746 g, 0.7 mmol) was dissolved in dimethyl sulfoxide (5 mL) and acetic anhydride (2.5 mL) was added. Triethylamine (2.3 mL, 16.5 mmol) was added at room temperature, the mixture refrigerated for 41 h, and then poured into cold, saturated sodium carbonate solution (100 mL) and extracted with chloroform (5 × 20 mL). The organic solutions was washed with brine (50 mL), dried, and evaporated. Separation of the components of the mixture by preparative t.l.c. (3:1 light petroleum–ethyl acetate) yielded **3** as white crystals, (0.1774 g, 58%).

The yield of the reaction was not affected when reaction was conducted under nitrogen, even though the mixture is less highly coloured when air is excluded.

*Methyl 4,6-*O*-benzylidene-α-*D*-glucopyranoside*. — The enol ester **3** (0.5079 g, 1.19 mmol) was suspended in methanol (10 mL), sodium borohydride (0.0970 g, 2.60 mmol) was added, and the mixture was stirred at room temperature. After 15 min, a solution was obtained. More sodium borohydride (0.1821 g, 4.8 mmol) was added, the mixture was stirred for 2 h, and it was then poured into brine. This solution was extracted with ethyl acetate (100 mL) and the organic solution washed with brine (100 mL), dried, and evaporated to give white crystals (0.4230 g). Trituration with cold light petroleum followed by cold benzene left white crystals of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (0.2044 g). The organic solutions were concentrated and the product purified by preparative t.l.c. (1:1 light petroleum–

ethyl acetate) to yield more methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (0.0354 g). The total weight of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside obtained was (0.2398 g, 71%).

*Methyl 2-O-acetyl-4-O-benzoyl-α-*D-ribo-*hexopyranosid-3-ulose* (**4**). — A solution of the enol ester **3** (0.2668 g, 0.626 mmol) in methanol (50 mL) was irradiated by sunlight for 65 h, whereupon it was concentrated to a colourless gum (0.2502 g) having the odor of benzaldehyde. Purification by preparative t.l.c. (1:1 light petroleum–ethyl acetate) provided benzaldehyde, starting material (**3**, 0.0438 g, 16%), and **4** (0.1398 g, 83% based on reacted starting material). Compound **4** was recrystallized from chloroform–light petroleum to yield fine, white needles m.p. 151–153°, ν_{max} 3475, 1722, and 1742 cm^{-1} and signals in the n.m.r. spectrum at δ 2.17 and 3.43 (each 3 H, s, $COCH_3$ and OCH_3 respectively), 2.90 (1 H, m, exchanged with D_2O), 3.87 (2 H, m, H-6 and H-6′), 4.17 (1 H, doublet of triplets, $J_{4,5}$ 10.0 and $J_{5,6}$ 2.5 Hz, H-5), 5.20 (1 H, d, J 4.0 Hz, H-1), 5.48 (1 H, d, J 4.0 Hz, H-2), 5.68 (1 H, d, J 10.0 Hz, H-4), 7.47 (3 H, m), and 8.00 (2 H, m).

Anal. Calc. for $C_{16}H_{18}O_8$: C, 56.80; H, 5.36; O, 37.84. Found: C, 56.40; H, 5.46; O, 38.14.

REFERENCES

1 D. Horton and E. K. Just, *Carbohydr. Res.*, 18 (1971) 81–94.
2 D. Bellus, *Adv. Photochem.*, 8 (1971) 109–159.
3 K. Mikami, K. Sato, C. Shin and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, 49 (1976) 1686–1689.
4 S. Hanessian and A. Staub, *Chem. Ind.* (*London*), (1970) 1436.
5 Compare R. U. Lemieux and G. Kotowycz, *Chem. Rev.*, 73 (1973) 669–698, and M. Barfield and S. Sternhell, *J. Am. Chem. Soc.*, 94 (1972) 1905–1913.
6 B. Coxon, *Tetrahedron*, 21 (1965) 3481–3503.