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STRUCTURAL CHANGES IN THE ACYLATION OF KETOSES. 1,2,3,4,5,6-HEXA-*O*-BENZOYL-L-*xylo*-HEX-1-ENITOL FROM L-SORBOSE

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ABSTRACT

Benzoylation of L-sorbose at room temperature with an excess of benzoyl chloride in pyridine gave a mixture of unsaturated cyclic and acyclic benzoates. The synthesis, and the structure of the title compound based on spectroscopic and ozonolysis studies, are reported. Ethyl 2,3,4,5-tetra-*O*-benzoyl-L-xylonate is also described, as well as the mass spectra of these acyclic benzoates.

INTRODUCTION

In a previous report[1] was described the synthesis of 1,3,5-tri-*O*-benzoyl-α-L-sorbopyranose (42.8%) and 1,3,4,5-tetra-*O*-benzoyl-α-L-sorbopyranose[2] (23.4%) by benzoylation of L-sorbose (L-*xylo*-2-hexulose; **1**) at −10° in pyridine with a 1:4 molar proportion of sugar to benzoyl chloride.

When this reaction was conducted with an excess of benzoyl chloride at room temperature and a further short heating at 100°, rearrangements and eliminations took place, affording cyclic benzoates and an acyclic, unsaturated benzoate. The structure and spectral characteristics of the latter, namely 1,2,3,4,5,6-hexa-*O*-benzoyl-L-*xylo*-hex-1-enitol (**2**), will be described in this paper.

RESULTS AND DISCUSSION

The formation of compound **2** can be explained by benzoylation of the 1,2-enediol form of *keto*-L-sorbose (**1**). The configuration of the double bond was not ascertained experimentally, but could be postulated as *Z* on the basis of fewer steric interactions.

When dissolved in ethanol, the syrup obtained by benzoylation of **1** under the new conditions gave crystalline **2** as prisms in 14.9% yield. The i.r. spectrum showed bands corresponding to enolic benzoate carbonyl group (1740 cm^{-1}), benzoic ester carbonyl group (1720 cm^{-1}), aliphatic double bond (1600 cm^{-1}), and those expected from the benzoate substituents.

The 60-MHz, n.m.r. spectrum of **2** in deuterated acetone showed resonances

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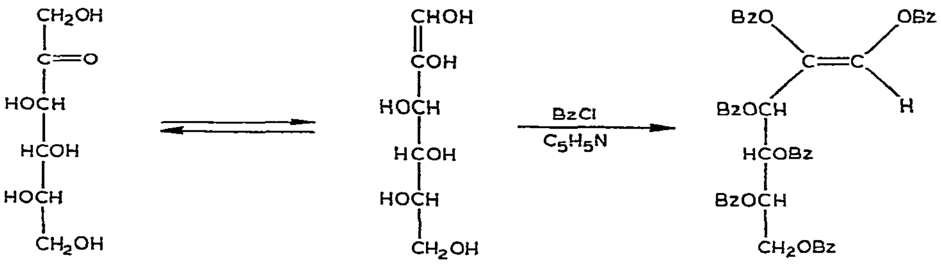


1 2

at τ 1.70–2.90 for six benzoyl groups that enclosed the signal of H-1. At τ 5.30, the C-6 methylene group appeared as a two-proton doublet, and, at τ 3.80, an H-3,4,5 multiplet that, at 100 MHz, was expanded slightly, but not improved in its resolution.

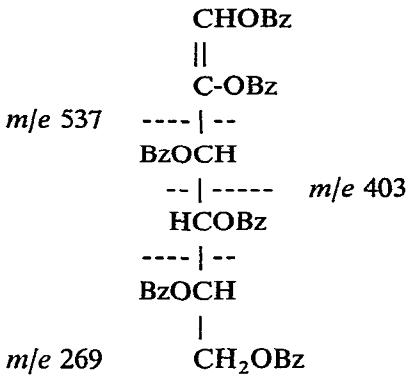
The mass spectrum (see Table I) of compound **2** showed fragmentation for a chain substituted with benzoyloxy groups, *i.e.*, the most intense peaks result from ruptures of benzoyl and benzoyloxy groups, or elimination of benzoic acid. The carbon skeleton gave intense peaks (at *m/e* 537 and 403) resulting from α- and β-cleavage, respectively, and the important protonated ion at 404. Further fragmentation of the *m/e* 537 peak, with loss of C-6, would give the intense peaks at *m/e* 416 and 415. The γ-rupture, to give *m/e* 269 (3%), appears to be of lesser importance.

TABLE I

MAJOR FRAGMENTS RESULTING FROM ELECTRON-IMPACT IONIZATION OF COMPOUND **2**

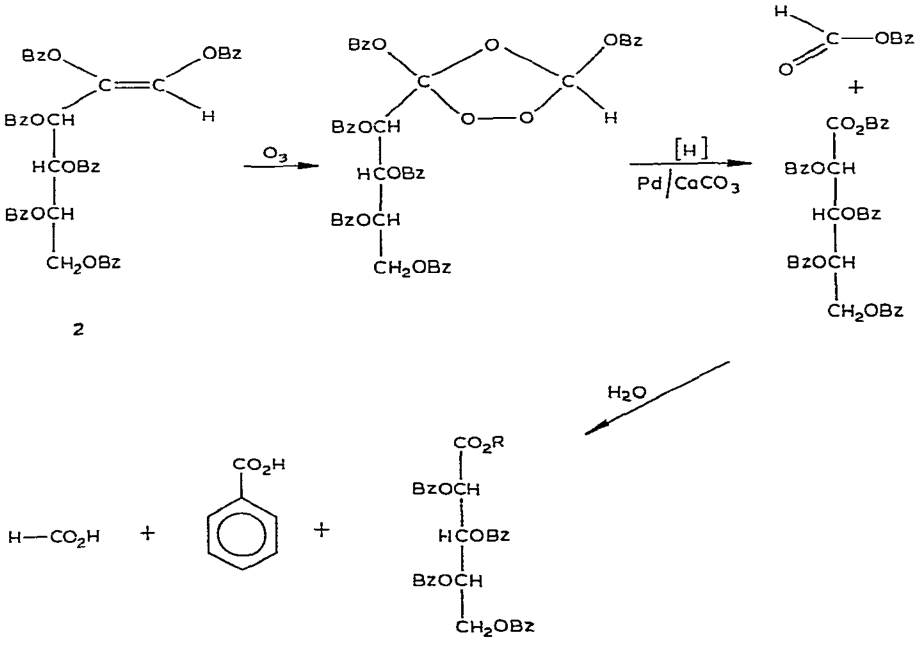
m/e	*Intensity (%)*[a]	*Assignments*[b]
804	—	M
699	3	M − Bz
682	7.5	M − BzOH
579	51.5	M − Bz − BzOH
537	14	M − (CHOBz=COBz)
474	18	M − 2 Bz − BzOH
457	47	M − Bz − 2 BzO
439	46	M − BzO − 2 BzOH
416	71	M − (CHOBz=COBz) − BzO
415	69.5	M − (CHOBz=COBz) − BzOH
404	57	$(CHOBz\text{-}CHOBz\text{-}CH_2OBz + H)^+$
403	32	$(CHOBz\text{-}CHOBz\text{-}CH_2OBz)^+$
402	29	$(CHOBz\text{-}CHOBz\text{-}CHOBz)^+$
335	12	M − Bz − 2 BzO − BzOH
334	50	M − Bz − BzO − 2 BzOH
331	6	$(Bz)_3^+$
269	3	$^+CHOBz\text{-}CH_2OBz$
122	16.5	BzOH
105	100.0	Bz^+

[a] Expressed as percent of the base peak. [b] Assignments are assumed.



The reductive ozonolysis of **2** is shown in Scheme 1. The aqueous solution containing formic and benzoic acids was made neutral and evaporated to dryness, and the mixture of salts was identified by paper chromatography. The n.m.r. spectrum of this mixture in D_2O showed a strong peak at τ 1.60 for the proton of the formate ion. The location of the double bond as being at C-1 in **2** was thus ascertained.

2,3,4,5-Tetra-*O*-benzoyl-L-xylonic acid (**3**), not hitherto described in the literature, was obtained as a syrup, and purified by preparative t.l.c. It was extracted from the plates with hot ethanol as the ethyl ester **3a**. Its structure, determined spectroscopically, confirmed the acyclic structure assigned to compound **2**.



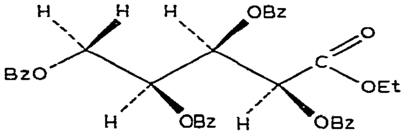
2

3 R = H

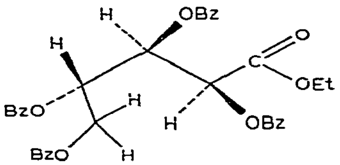
3a R = Et

Scheme 1

In the n.m.r. spectrum of **3**, in contrast with that of **2**, the resonances of each proton were readily recognizable. At τ 8.80 and 5.80, the methyl triplet and the methylene quartet of the esterifying ethyl group appeared. The C-5 methylene group resonated as a poorly resolved multiplet at τ 5.27; the signal of H-2 at τ 4.21 appeared as a doublet ($J_{2,3}$ 3.5 Hz), and that of H-3 at τ 3.67 as a pair of doublets ($J_{3,4}$ 6 Hz). H-4 resonated as an unresolved, broad multiplet, centered at τ 3.97, that suggested large coupling-constants. The values of $J_{2,3}$ and $J_{3,4}$ agree with those for a favored, sickle conformation[2], in which the 1,3-parallel interaction of the 2- and 4-*O*-benzoyl groups present in the planar, zigzag conformation **3b** is alleviated by rotation about the C-3–C-4 bond so as to locate H-3 and H-4 in an almost antiparallel orientation (**3c**). Similar observations have been made on acyclic derivatives having the *xylo* configuration[2,3].



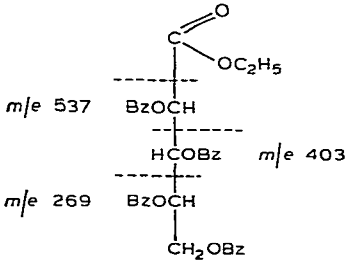
3b



3c

As a true, antiparallel relationship of H-3 and H-4 would imply a J value of ~8 Hz, the real situation for compound **3** in solution would be such that, while the sickle structure preponderates, minor contributions from the alternative, C-3–C-4 rotamers are also present. The expanded, H-4 multiplet suggests that the C-4–C-5 rotamer having H-4 bisecting the angle of the C-5 methylene group makes no significant contribution.

The mass spectrum of **3** (see Table II) shows the structurally significant peaks at *m/e* 537, 403, and 269 originated by α-, β-, and γ-fragmentations of the acyclic chain. The other peaks are foreseeable as caused by rupture of the benzoate substituents.



EXPERIMENTAL

General procedures. — T.l.c. was performed on Silica Gel G (Merck). Paper chromatography was conducted on Whatman No. 1 paper by the descending tech-

TABLE II

MAJOR FRAGMENTS RESULTING FROM ELECTRON-IMPACT IONIZATION OF COMPOUND 3

m/e	*Intensity (%)*[a]	*Assignments*[b]
610	—	M
565	1	$M - OC_2H_5$
537	3	$M - CO_2C_2H_5$
488	15	$M - OC_2H_5 - C_6H_5$
403	23	$(CHOBz\text{-}CHOBz\text{-}CH_2OBz)^+$
383	4	$M - OC_2H_5 - C_6H_5 - C_6H_5CO$
367	7	$M - OC_2H_5 - C_6H_5CO_2$.
366	22	$M - OC_2H_5 - C_6H_5 - BzOH$
311	4	$(CHO\text{-}CH\text{-}CHOBz\text{-}CH_2OBz)^+$
281	8	$(CH{=}COBz\text{-}CH_2OBz)^+$
269	17	$(CHOBz\text{-}CH_2OBz)^+$
262	13	$(CO\text{-}CO_2CHOH\text{-}CHO\text{-}CH_2OBz)^+$
245	3	$(OC\text{-}CO_2C\text{-}CH\text{-}CH\text{-}CH_2OBz)^+$
122	5	BzOH
77	100	$C_6H_5^+$

[a]Expressed as percent of the base peak. [b]Assignments are assumed.

nique. The solvents employed were (*A*) 99:1 (v/v) benzene–methanol, and (*B*) 7:1:3 (v/v) 2-propanol–ammonia–water. The spray reagents were (*C*) alkaline hydroxylamine–ferric nitrate for esters[4], and (*D*) sulfanilamide–2-naphthol for acids[5]. Melting points (Kofler hot-stage) are not corrected. Optical rotations were determined at 20° with a Perkin–Elmer 141 polarimeter. I.r. spectra were recorded, for Nujol mulls, with a Perkin–Elmer 137-B Infracord spectrophotometer. U.v. spectra were recorded, for ethanolic solutions, with a Beckman DK2-A spectrophotometer. N.m.r. spectra of benzoates were recorded at 20–25°, at 60 MHz, with a Varian A-60 spectrometer, with tetramethylsilane as the internal reference-standard. Coupling constants are first-order measurements. Mass spectra were recorded with a Varian-Mat CH-7 spectrometer commanded by a Varian-Mat Data System 166 computer, at an ionizing potential of 70 eV; the temperature of the direct-insertion probe was 150–180°.

*Hexa-O-benzoyl-*L-xylo*-hex-1-enitol* (**2**). — A mixture of benzoyl chloride (210 mL, 1.8 mol) and pyridine (410 mL) was cooled to —10° and L-sorbose (18 g, 0.1 mol) was slowly added. The solution was shaken for 48 h at room temperature, and was then heated for 1 h in a water bath at 100°. After being cooled, the solution was poured into ice–water (3 L), and the syrup obtained was washed repeatedly with cold, and warm, water. The residue was dissolved in chloroform, and the solution was washed successively with a saturated solution of sodium hydrogencarbonate, and water, dried (anhydrous sodium sulfate), and evaporated to dryness; the residue (64 g) was dissolved in boiling ethanol, the solution decolorized (charcoal), and, on cooling, a white solid (15 g), m.p. 125°, was obtained. Recrystallization from ethanol gave 12 g (14.9%) of **2** as prisms, m.p. 133–134°, $[\alpha]_D$ —43.1° (*c* 0.5, chloroform); in t.l.c. (solvent *A*, reagent *C*), it showed only one spot, R_F 0.61; λ_{max} 230 nm (ε_{mM}

18.60); n.m.r.: τ 5.30 (CH_2), 3.80 (m, H-3,4,5), and 1.70–2.90 (m, 6 benzoyl groups and H-1).

Anal. Calc. for $C_{48}H_{36}O_{12}$: C, 71.64; H, 4.47. Found: C, 71.61; H, 4.21.

Concentration of the mother liquors of recrystallization of **2** gave plates (1.4 g), m.p. 161°, $[\alpha]_D$ +1.4° (*c* 0.5, ethyl acetate). On the other hand, after separation of **2**, evaporation of the ethanolic solution left an uncrystallizable syrup (49 g) whose composition, as well as the structure of the compound having m.p. 161°, will be the subject of a future report.

Ozonolysis of **2**. — Compound **2** (500 mg) was dissolved in ethyl acetate (50 mL), and ozonized during 1 h at —70° (acetone–Dry Ice). The excess of ozone was then removed by a stream of air, and the solution was shaken for 1 h in an atmosphere of hydrogen in the presence of 10% Pd-on-calcium carbonate (200 mg). After filtration of the suspension, the filtrate was evaporated to dryness, and the residue was macerated with cold water (35 mL) for 24 h. The aqueous layer was decanted from the white, syrupy residue, and this was washed with cold (20 mL) and warm water (2 × 5 mL), and dried in a vacuum desiccator.

The aqueous solutions were combined, made neutral with 0.1M sodium hydroxide (to the Phenol Red end-point), and evaporated to dryness. The saline residue, in paper chromatography (solvent *B*, reagent *D*), showed two spots (R_F 0.6 and 0.70) coincident with those of sodium formate and sodium benzoate, respectively. The n.m.r. spectrum of this mixture in D_2O showed the aromatic peaks of benzoate ions, and a strong singlet for the formate-ion proton at τ 1.60.

Ethyl 2,3,4,5-tetra-O-benzoyl-L-xylonate (**3**). — The water-insoluble syrup from the ozonolysis (290 mg) was purified by preparative t.l.c. (solvent *A*; u.v. detection). The principal band (R_F 0.64) was extracted with hot ethanol and, after evaporation of the solvent, chromatographically pure **3** was obtained as a syrup, $[\alpha]_D$ +46.7° (*c* 1.1, methanol); n.m.r.: τ 8.80 (t, CH_3), 5.80 (q, CH_2), 4.73 (m, H-5,5'), 4.21 (d, H-2, $J_{2,3}$ 3.5 Hz), 3.67 (dd, H-3, $J_{3,4}$ 6 Hz), and 3.97 (m, H-4).

Anal. Calc. for $C_{35}H_{30}O_{10}$: C, 68.85; H, 4.91. Found: C, 68.87; H, 5.15.

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