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Bromination of sugar enones and enonolactones

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Abstract

Bromination of 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*erytro*-hex-2-enono-1,5-lactone (**1**) took place diastereoselectively to afford a single product: 2,4,6-tri-*O*-benzoyl-2,3-dibromo-3-deoxy-D-altrono-1,5-lactone (**2**). The configuration of C-2 and C-3 was determined as *R,R* by NMR spectroscopy and taking into account considerations of the stereochemical course of the bromination. The configuration of **2** was confirmed by X-ray analysis, which also revealed that the conformation of the lactone ring consists of a $^4H_3$(D) distorted half-chair. The bromine addition to 2,5,6,7-tetra-*O*-benzoyl-D-*arabino*-hept-2-enono-1,4-lactone (**5**), readily prepared by DBU-promoted elimination from the perbenzoylated lactone derivative **4**, was also diastereoselective and led to the dibromo derivative **6**, whose configuration for C-2 and C-3 was assigned as *S,S*. Bromination of the α,β-unsaturated carbonyl system of 2-propyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**7**) afforded an unsaturated monobromo derivative: 2-propyl 6-*O*-acetyl-3-bromo-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**8**), suggesting that dehydrobromination occurred after addition of bromine.

Keywords: Bromination; Sugar enones and enonolactones; Enones; Enonolactones

1. Introduction

2-Bromo-2-deoxy-aldono-1,4-lactones are readily available from aldonic acids, and are useful intermediates in the synthesis of α- and β-amino polyhydroxy acids [1].

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Table 1
^{13}C NMR chemical shifts (δ) for compounds **2**, **5**, **6**, and **8**

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7
2	160.4	76.5	53.8	64.3	77.3	62.0	
5	162.4	138.9	129.5	77.2	70.5 [a]	69.1 [a]	62.5
6	162.5	78.5	54.1	76.9	72.7 [a]	69.7 [a]	61.8
8	97.7	185.4	121.4	150.2	70.5	66.7	

[a] Signals may be interchanged.

Recently, a free radical-induced *C*-allylation of α-bromolactones, to give 2-*C*-allyl-2-deoxy-aldopentono-1,4-lactones, was described [2]. On the other hand, unexpected substitutions were reported to occur [3] when 3-(1-hydroxyalkyl)-2(5*H*)-furanones were treated with bromine, and it was also observed that several α-methylene-γ-butyrolactones did not add bromine efficiently [4]. In view of these results, and taking into account the interesting reactivity of α-bromolactones, we studied the bromination of α,β-unsaturated furanones and pyranones derived from sugars. The products of bromination constitute valuable intermediates for the synthesis of 3-bromo-3-deoxy-2-ketoaldonic acids, precursors of specifically labeled (^2H or ^3H) 3-deoxy-2-ketoaldonic acids with a defined stereochemistry on C-3. Such compounds may be employed for the elucidation of biosynthetic pathways. Furthermore, brominated 2-(5*H*)-furanones are structures found in secondary metabolites of marine origin [5].

2. Results and discussion

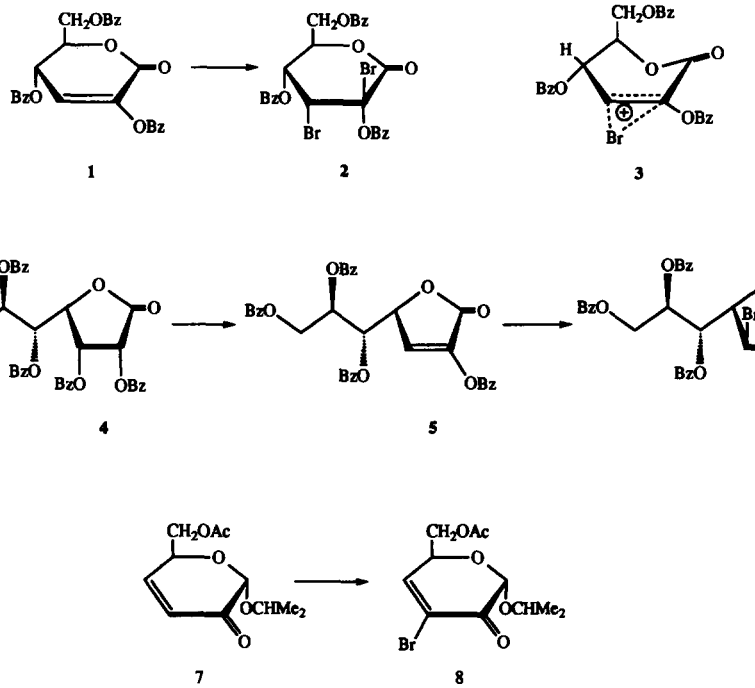
Prolonged benzoylation of D-glucono-1,5-lactone in the presence of pyridine gave [6] (> 90% yield) 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone (**1**) which, on bromination in the dark for 24 h, afforded the crystalline dibromide derivative **2**, in 87% yield. The bromination accelerates when the reaction mixture is irradiated with bright light. After 2 h of irradiation, **2** was obtained in 80% yield. In both cases, compound **2** was the only isomer, from the four theoretically possible, detected in the NMR spectra (Tables 1 and 2) of the bromination mixture. The presence of two bromine atoms in the molecule of **2** was evidenced by its ^{13}C NMR spectrum. Thus, the signal

Table 2
^1H NMR data for compounds **2**, **5**, **6**, and **8**

Compound	δ (ppm)							J (Hz)							
	H-3	H-4	H-5	H-6	H-6′	H-7	H-7′	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$
2	6.20	6.39	5.27	4.79	4.57			3.0	10.0	2.6	3.4	12.8			
5	[a]	5.59	← 6.02 →			5.03	4.58								12.5
6	5.77	5.31	6.30	5.92		5.00	4.61	3.0	8.5	3.6			5.4	5.5	12.0
8 [b]		7.33	4.83	4.38	4.20				1.9	5.4	5.3	11.8			

[a] Overlapped with H-aromatic.
[b] $\delta_{H\text{-}1}$ 5.15.

for C-2 appeared at higher fields (δ 76.5) than the C-2 resonance [7] of 2,3,4,6-tetra-*O*-benzoyl-2-bromo-D-glucono-1,5-lactone (δ 84.1), and the C-3 gave a signal at a δ value (53.8 ppm) characteristic of a bromine-substituted carbon atom. The electron impact-mass spectrum (EIMS) of **2** showed only monobrominated ions and no dibrominated ions. The pair of ions of highest m/z appeared at 324 and 326, which would originate from $M^{+\cdot}$ by loss of benzoyl bromide and benzoic acid. The subsequent loss of benzoic acid and carbon monoxide would lead to the fragments at m/z 202 and 204, and 174 and 176, respectively.



1 2 3

4 5 6

7 8

The approach of bromine to the π system of the enol ether is expected to occur from the side of the molecule opposite to the benzoyloxymethyl group. Such stereoselectivity was previously observed [6] in the addition of hydrogen to the double bond of **1** and it was attributed to the fact that in its preferred ^5H_O conformation, the benzoyloxymethyl group is axially oriented, preventing the approach of hydrogen from above the molecular plane [6,8]. Similarly, the atack of bromine would take place from the less hindered side of the molecule, leading to charge-transfer complexes that may rearrange to intermediate ions [9]. In this case, the charge stabilization by the benzoyloxy substituent on C-2 would induce the formation [10] of a weakly bridged bromonium ion intermediate **3**, and the attack of bromide on C-2 from the opposite side (*trans*-opening). Therefore, an *R,R* configuration may by expected for C-2 and C-3.

The stereochemistry 2(*R*), 3(*R*) was confirmed by X-ray diffraction analysis (Fig. 1)

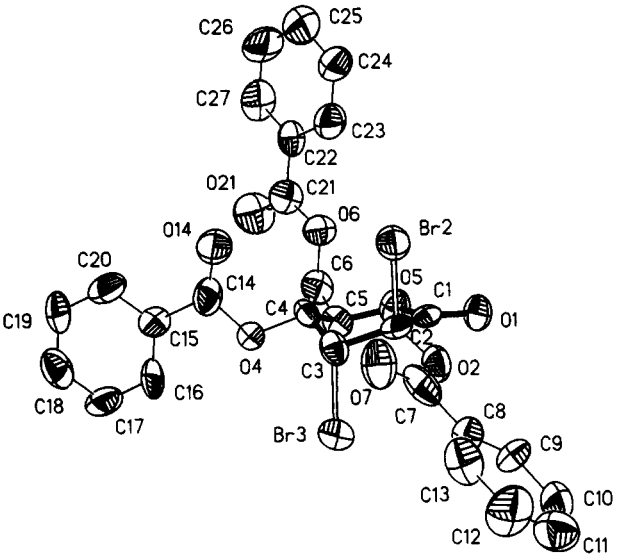


Fig. 1. Schematic drawing (XP in SHELXTL-PC package [22]) of 2,4,6-tri-*O*-benzoyl-2,3-dibromo-3-deoxy-D-altrono-1,5-lactone (**2**) with the numbering scheme used. Thermal displacement ellipsoids are shown at a level of 50%.

of an acceptable crystal of **2**, which was obtained from 2-propanol after many weeks of intensive attempts at recrystallization. In spite of the rather poor diffracting power of the crystal, for our purposes, the resolution of the structure could be satisfactorily accomplished. Data collection information, as well as details on the structure resolution and refinement are described in Table 3, while Table 4 shows atomic positions and equivalent isotropic temperature factors. Because of the quality of the data set, the values of distances and angles were calculated with rather high ESDs (typical values: 0.02 Å and 1°, respectively) but they do not differ from commonly accepted values. Table 5 quotes selected values for torsion angles. The packing diagram (Fig. 2) showed a short Br-2 · · · O-1 [3.07(2) Å] intermolecular contact, and two O · · · H-C distances slightly below the sum of the corresponding Van der Waals radii [O-14 · · · H-5a(-C-5): 2.39(3) Å, O-7 · · · H-26(-C-26): 2.36(3) Å]. The X-ray structural analysis of **2** revealed that the two bromine substituents are *anti*, with a torsional angle between them of −167.3°. The Br-3 substituent is axially oriented, and the torsional angles C-2–C-3–C-4–C-5 (59°) and C-3–C-4–C-5–O-5 (−55°) show small distorsions with respect to the $^4C_1$ chair conformation for this region. However, the torsion angles around C-1 show substantial deviation from mean values, i.e., 22° for C-3–C-2–C-1–O-5 and −18° for C-2–C-1–O-5–C-5, resulting in a flattening of the chair at the C-1 segment. As shown for other lactones [11,12], the planarity of the carboxyl group of **2** does not extend to C-5, as has been predicted for the valence-bond representation of the resonance form C–C(O$^-$)=O$^+$–C. Thus, C-5 and C-3 are, respectively, 0.32 and 0.46 Å below the average plane determined by C-1, C-2, O-1, and O-5, whereas C-4 lies 0.11 Å above this plane. The conformation of the 1,5-lactone ring of **2** can be described as a $^4H_3$

Table 3
Crystal data and structural determination and refinement data for **2**

Crystal data:
Molecular formula: $C_{27}H_{20}Br_2O_8$; mol wt 632.25; Orthorhombic, $P2_12_12_1$ (no. 19), $Z = 4$.
Cell dimensions (Å, at 293 K): $a = 6.055(2)$, $b = 20.725(5)$, $c = 21.013(5)$.
V (Å^3) = 2636.9(12): D_x (g cm^{-3}) = 1.59.
Structure determination and refinement data:
Crystal dimensions (mm): 0.44×0.12×0.06, colorless prisms.
Number of reflections measured: 2032 (23 rejected) (Siemens P4 diffractometer, $\omega/2\theta$ scan).
Number of unique reflections: 2009.
Number of reflections with $[F^2/\sigma(F^2)] > 2$: 1106 (55%). Average $[F^2/\sigma(F^2)]$: 9.2.
θ range (°): 1.94–22.55, index range: $0 \le h \le 6$, $0 \le k \le 22$, $0 \le l \le 22$.
Radiation: MoK_α ($\lambda = 0.71073$ Å, graphite monocromator), μ (mm^{-1}) = 3.12.
Max/min semi-empirical absorption corrections (ψ scan): 0.694/0.612.
No extinction correction applied.
Structure solution:
Direct methods plus difference Fourier (SHELX-86) [a]. Hydrogen atoms placed at expected positions.
Structure refinement:
(SHELXL-93) [b] Weighted [c] full-matrix least-squares on F^2, for the whole unique data set .
Phenyl groups constrained to idealized D_{6h} geometry [regular hexagons, d(C–C) = 1.39 Å, one independent pivot atom attached to the structure plus three rotational degrees of freedom].
Anisotropic displacement factors for non-H atoms. Observation to parameter ratio: 6.7.
Final agreement factors:
Goodness-of-fit on F^2: $[F^2 > 2\sigma(F^2)]$: 1.067 [all data]: 0.988.
$R_1(F)$ [d], $wR_2(F^2)$ [e] $[F^2 > 2\sigma(F^2)]$: 0.053, 0.073 [all data]: 0.136, 0.099.
Maximum peak, hole in final difference Fourier map: 0.36, −0.30 eÅ^{-3}.

[a] See [23].
[b] See [24].
[c] $w = 1/[s^2(F_o^2) + (0.0217P)^2 + 4.4947P]$, $P = (F_o^2 + 2F_c^2)/3$.
[d] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.
[e] $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$.

distorted half-chair. Crystalline D-glucono-1,5-lactone exhibits a similar conformation [11].

The conformation of **2** in solution is like that found in the solid state. Thus, the $J_{4,5}$ (10.0 Hz) and $J_{3,4}$ (3.0 Hz) indicate an *anti* and *gauche* disposition for the respective coupled protons, which agree with a $^4H_3$ conformation for **2**. This form is essentialy free of non-bonding interactions. The conformation of the aldono-1,5-lactone ring in solution has been described as an equilibrium between half chair ($^3H_4$ or $^4H_3$) and boat [$B_{2,5}$(D)] forms [13,14]. The position of the equilibrium would be determined by non-bonding interactions in each individual conformer [13]. In the case of **2** the $^3H_4$ conformation shows an eclipsing interaction between the BzO-2 group and the Br atom at C-3. A similar destabilizing effect between Br-3 and BzO-4 and also two *gauche* interactions of Br-3 and the substituents at C-2 are expected for a $B_{2,5}$ conformation. Furthermore, the small $J_{5,6}$ and $J_{5,6'}$ values suggested a *g,g* conformation for the lateral chain of **2**, as reported for other aldono-1,5-lactones [14]. The same conformation around the C-5–C-6 bond is observed in the crystalline state, as the dihedral angles O-5–C-5–C-6–O-6 and C-4–C-5–C-6–O-6 are, respectively, −66 and 57°.

Table 4
Atomic coordinates [$\times 10^4$] and equivalent isotropic displacement parameters [$Å^2 \times 10^3$] for **2**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	x	y	z	U_{eq}
Br-2	375(2)	8475(1)	−7(1)	65(1)
Br-3	−4773(3)	9563(1)	1216(1)	74(1)
O-1	−4892(17)	8253(5)	−436(4)	63(3)
O-2	−3392(17)	8232(4)	738(5)	58(3)
O-4	−1692(17)	10507(5)	473(4)	61(3)
O-5	−4342(17)	9297(5)	−542(4)	63(3)
O-6	−1677(18)	10177(4)	−1174(5)	62(3)
O-7	−662(19)	8309(5)	1472(5)	77(4)
O-14	1571(17)	10666(5)	−9(7)	96(4)
O-21	−1160(21)	11184(5)	−1514(6)	108(5)
C-1	−4032(22)	8731(8)	−222(8)	47(5)
C-2	−2531(24)	8724(8)	363(8)	56(5)
C-3	−2188(25)	9379(6)	679(6)	50(4)
C-4	−1869(24)	9883(6)	176(6)	44(4)
C-5	−3833(27)	9923(8)	−265(7)	59(5)
C-6	−3571(25)	10371(7)	−819(7)	64(5)
C-7	−2431(25)	8097(7)	1307(7)	66(5)
C-8	−3736(16)	7632(5)	1689(4)	72(6)
C-9	−5766(17)	7413(5)	1467(4)	70(6)
C-10	−6952(16)	6961(5)	1816(6)	82(6)
C-11	−6108(22)	6727(4)	2386(5)	91(7)
C-12	−4079(23)	6946(5)	2608(4)	96(7)
C-13	−2893(16)	7398(5)	2259(5)	70(5)
C-14	126(26)	10864(6)	321(7)	64(5)
C-15	60(15)	11523(3)	593(4)	50(4)
C-16	−1784(14)	11729(4)	931(4)	64(5)
C-17	-1839(19)	12347(5)	1188(4)	88(6)
C-18	−51(24)	12759(4)	1107(5)	81(6)
C-19	1793(19)	12553(5)	769(5)	81(6)
C-20	1848(13)	11935(5)	512(4)	72(5)
C-21	−642(24)	10635(7)	−1522(7)	68(5)
C-22	1277(15)	10378(4)	−1878(4)	55(5)
C-23	1810(18)	9726(4)	−1839(5)	80(6)
C-24	3644(20)	9489(4)	−2160(5)	97(7)
C-25	4947(17)	9903(7)	−2521(5)	106(6)
C-26	4414(19)	10554(6)	−2560(4)	97(7)
C-27	2579(19)	10792(4)	−2239(5)	79(6)

Benzoylation of D-*glycero*-D-*gulo*-heptono-1,4-lactone [15] with benzoyl chloride–pyridine for 2 h, afforded the crystalline perbenzoyl derivative **4**. Monoelimination of benzoic acid from **4**, promoted by diazabicyclo[5.4.0]undec-7-ene (15 min, 0°C), afforded 2,5,6,7-tetra-*O*-benzoyl-D-*arabino*-hept-2-enono-1,4-lactone (**5**) in 67% yield. This procedure is clearly advantageous over that previously described [16], based on the prolonged benzoylation of the free lactone, which led to **5** in 24% yield.

The double bond of **5** was less reactive, in the bromination reaction, than that of the 2-enono-1,5-lactone derivative **1**. However, on treatment of **5** with bromine in

Table 5
Selected torsion angles [°] for **2**

C-5–O-5–C-1–O-1	166(1)	C-3–C-4–C-5–C-6	−175(1)
C-5–O-5–C-1–C-2	−18(2)	C-21–O-6–C-6–C-5	−154(1)
C-7–O-2–C-2–C-3	−52(2)	O-5–C-5–C-6–O-6	−66(2)
C-7–O-2–C-2–C-1	−180(1)	C-4–C-5–C-6–O-6	57(2)
C-7–O-2–C-2–Br-2	71(1)	C-2–O-2–C-7–O-7	−12(2)
O-1–C-1–C-2–O-2	−32(2)	C-2–O-2–C-7–C-8	171(1)
O-5–C-1–C-2–O-2	151(1)	O-7–C-7–C-8–C-9	180(1)
O-1–C-1–C-2–C-3	−162(1)	O-2–C-7–C-8–C-9	−4(2)
O-5–C-1–C-2–C-3	22(2)	O-7–C-7–C-8–C-13	−2(2)
O-1–C-1–C-2–Br-2	84(2)	O-2–C-7–C-8–C-13	174(1)
O-5–C-1–C-2–Br-2	−93(1)	C-7–C-8–C-9–C-10	178(1)
O-2–C-2–C-3–C-4	−164(1)	C-7–C-8–C-13–C-12	−178(1)
C-1–C-2–C-3–C-4	−42(2)	C-4–O-4–C-14–O-14	−4(2)
Br-2–C-2–C-3–C-4	70(1)	C-4–O-4–C-14–C-15	174(1)
O-2–C-2–C-3–Br-3	−42(2)	O-14–C-14–C-15–C-16	175(1)
C-1–C-2–C-3–Br-3	80(1)	O-4–C-14–C-15–C-16	−3(2)
Br-2–C-2–C-3–Br-3	−167(1)	O-14–C-14–C-15–C-20	−6(2)
C-14–O-4–C-4–C-3	126(1)	O-4–C-14–C-15–C-20	176(1)
C-14–O-4–C-4–C-5	−113(1)	C-14–C-15–C-16–C-17	180(1)
C-2–C-3–C-4–O-4	176(1)	C-14–C-15–C-20–C-19	−180(1)
Br-3–C-3–C-4–O-4	56(1)	C-6–O-6–C-21–O-21	4(2)
C-2–C-3–C-4–C-5	59(2)	C-6–O-6–C-21–C-22	−179(1)
Br-3–C-3–C-4–C-5	−61(1)	O-21–C-21–C-22–C-23	177(1)
C-1–O-5–C-5–C-6	159(1)	O-6–C-21–C-22–C-23	1(2)
C-1–O-5–C-5–C-4	34(2)	O-21–C-21–C-22–C-27	−1(2)
O-4–C-4–C-5–O-5	−174(1)	O-6–C-21–C-22–C-27	−177(1)
C-3–C-4–C-5–O-5	−55(2)	C-21–C-22–C-23–C-24	−178(1)
O-4–C-4–C-5–C-6	67(2)	C-21–C-22–C-27–C-26	178(1)

dichloromethane, under bright light, the dibromo derivative **6** was obtained. The yield of **6** increased to ~50% when the reaction temperature was maintained at −15°C. The product was unstable and in solution (even during the recrystallization) partially reverted to the starting enonolactone **5**.

The ^{13}C NMR spectrum of **6** showed the resonances of the brominated carbons at 78.6 (C-2) and 54.3 ppm (C-3). The MS of **6** gave a pattern of fragmentations similar to that observed for **2**. Thus, the elimination of benzoyl bromide and benzoic acid from $M^{+\cdot}$ would lead to bromine containing ions at m/z 458 and 460. Further loss of benzoic acid would produce the ions at m/z 336 and 338, which by loss of a benzoyl radical and carbon dioxide give m/z 187 and 189. The ^1H NMR spectrum of **6** showed a doublet due to H-3 at δ 5.72 ($J_{3,4}$ 3.0 Hz) and the double doublet of H-4 at δ 5.26 ($J_{4,5}$ 8.5 Hz). Consideration of the steric course of the bromination indicates a preferred approach of the bromine atom from the face opposite the lateral chain of **5**, as described for other additions to the double bond of α,β-unsaturated-1,4-lactones [16,17]. The resulting weakly bridged bromonium ion would undergo *trans*-opening to give stereoselectively the dibromolactone **6**, having the 2(*S*), 3(*S*) configuration for the asymmetric centers generated during the bromination. In order to avoid *gauche* interactions with the

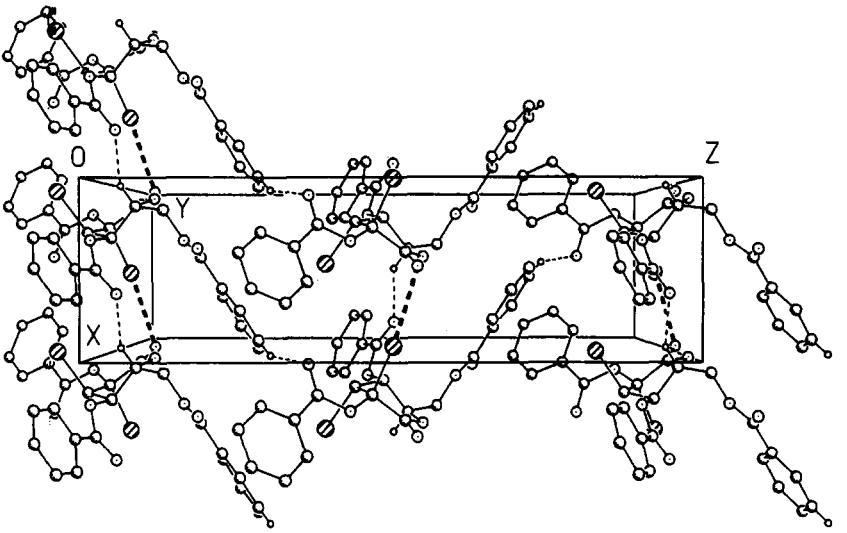


Fig. 2. Crystal packing of **2** (XP in SHELXTL-PC package [22]). Only H atoms involved in short contacts have been included.

substituents at C-2, the bromine atoms on C-2 and C-3 adopt axial orientations, and a ^3E conformation may be anticipated for **6**. The $J_{3,4}$ value is consistent with the dihedral angle between H-3 and H-4 expected for such a conformation, and also agrees with the $J_{3,4}$ value calculated by the modified Karplus equation described by Dana et al. [18], for 2-bromo-1,4-lactones.

The bromination of 2-propyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**7**), readily prepared [19] from 2-acetoxy-3,4,6-tri-*O*-acetyl-D-galactal, was also studied. The reaction took place rapidly at 0°C, to give a syrupy product, the MS of which showed the isotopic cluster of the molecular ion at 306 and 308 (1:1 ratio) characteristic of a monobrominated derivative. A retro Diels–Alder fragmentation of $M^{+\cdot}$ would give rise to the ions at m/z 218, 220, which would lead to m/z 176 and 178 (base peaks) by losing ketene. On the other hand, the elimination of the isopropyl anomeric subtituent would produce ions at m/z 247 and 249, which by further loss of ketene or acetic acid would lead to ions at m/z 205 and 207, and 187 and 189, respectively. In the ^{1}H NMR spectrum of the product, a signal for one vinylic proton (doublet at δ 7.33) was observed, suggesting that H-3 in **7** had been replaced by a bromine atom. The ^{13}C NMR APT [20] spectrum showed an opposite phase for the vinylic carbon signals, indicating that only one of those carbon atoms had a proton attached. Therefore, the structure for the bromination product of **7** was established as 2-propyl 6-*O*-acetyl-3-bromo-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**8**). The formation of an unsaturated monobromo derivative suggests that, after the addition of bromine to the double bond of **7**, dehydrobromination takes place, in order to regenerate the stable carbonyl α,β-unsaturated system. Similarly, levoglucosenone gave also, on bromination, an α-bromo-α,β-unsaturated derivative [21]. These results con-

trast with those obtained for the bromination of the pyranone **1** and the furanone **5**, to give, respectively, the dibromide derivatives **2** and **6**, which did not undergo further elimination. This behavior could be attributed to the lack of H-2 in **2** and **6**, which would prevent the dehydrobromination reaction.

3. Experimental

General methods.—Melting points were determined on a Fisher–Johns apparatus, and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. Nuclear magnetic resonance (NMR) spectra were determined on a Bruker AC 200 spectrometer at 200 MHz (^{1}H) or 50.3 MHz (^{13}C) for solutions in $CDCl_3$. The spectral data are given in Tables 1 and 2. The electron impact-mass spectra (EIMS) were obtained with a Trio-2 VG Masslab spectrometer, opperating at 20 eV. The crystal structure analysis was obtained on a Siemens P4 diffractometer at 293 K; a summary of the X-ray data is given in Table 3. Thin layer chromatography (TLC) was performed on aluminium plates precoated with Silica Gel 60 F_{254} (E. Merck), developed with the solvents indicated in each individual case. The spots were visualized by exposure to UV light and by charring the plates after spraying with 10% H_2SO_4 in EtOH.

*2,4,6-Tri-O-benzoyl-2,3-dibromo-3-deoxy-*D*-altrono-1,5-lactone* (**2**).—To a solution of 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone (**1**, 3.00 g, 6.36 mmol) in dry CH_2Cl_2 (50 mL), bromine (1.00 mL, 19.41 mmol) was added, and the mixture was stirred in the dark at room temperature. After 24 h, the mixture showed (TLC, 3:1 hexane–EtOAc) a single spot having R_f 0.48, and no starting material (**1**, R_f 0.38) remained. The mixture was diluted with CH_2Cl_2 (200 mL) and washed with saturated aqueous solutions of $NaHSO_3$ (75 mL), $NaHCO_3$ (2 × 100 mL), and NaCl (2 × 100 mL), dried ($MgSO_4$) and concentrated. The resulting syrup was recrystallized from 2-propanol to afford white crystals of **2** (3.48 g, 87%); mp 130–131°C; $[\alpha]_D$ +123° (*c* 1, $CHCl_3$); MS *m/z* (relative intensity %): 410 (0.5), 386 (0.4), 367 (0.5), 341 (1.3), 324, 326 (8.1), 219, 221 (15.4), 202, 204 (6.9), 174, 176 (16.2), 136 (13.4), 122 (43.8), 105 (100). Anal. Calcd for $C_{27}H_{20}Br_2O_8$: C, 51.29; H, 3.19. Found: C, 51.14; H, 3.54.

The bromination was also performed starting from **1** (0.61 g, 1.29 mmol), CH_2Cl_2 (20 mL), and bromine (0.2 mL). The mixture was irradiated with bright light (300 W, W lamp) for 2 h, whereupon a single spot of R_f 0.48 (3:1 hexane–EtOAc) was detected by TLC. The mixture was treated as already described to afford compound **2** (0.65 g, 80% after recrystallization from 2-propanol), which had the same physical constants and spectral properties as product **2**, previously described.

*2,5,6,7-Tetra-O-benzoyl-3-deoxy-*D-arabino-*hept-2-enono-1,4-lactone* (**5**).—To a cooled (−15°C) solution of 2,3,5,6,7-penta-*O*-benzoyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone [15] (**4**, 0.63 g, 0.86 mmol) in dry CH_2Cl_2 (15 mL), diazabicyclo[5.4.0]undec-7-ene (DBU, 0.13 mL, 0.86 mmol) was added dropwise with stirring. After 15 min the mixture showed (TLC, 3:1 hexane–EtOAc) no starting material R_f 0.29) and a main spot of R_f 0.38. The mixture was diluted with CH_2Cl_2 (100 mL) and washed with aq 10% HCl (50 mL) and then with satd aq NaCl (50 mL), $NaHCO_3$ (50 mL), and NaCl (50 mL). The organic extract was dried ($MgSO_4$) and concentrated, affording a

pale-brown syrup, which crystallized upon addition of EtOH. Recrystallization from the same solvent afforded **5** (0.35 g, 67%); mp 181–182°C; lit. [16] mp 181–182°C.

2,5,6,7-Tetra-O-*benzoyl-2,3-dibromo-3-deoxy*-D-glycero-D-galacto-*heptono-1,4-lactone* (**6**).—To a solution of 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*arabino*-hept-2-enono-1,4-lactone (**5**, 0.16 g, 0.27 mmol) in dry CH_2Cl_2 (15 mL), bromine (0.20 mL, 4 mmol) was added. The mixture was cooled to −15°C (NaCl–ice) and irradiated with bright light (300 W, W lamp). After 7 h TLC examination (3:1 hexane–EtOAc) showed complete conversion of **5** (R_f 0.34) into a less polar compound (R_f 0.42). The mixture was subjected to the same treatment applied in the purification of **2**, but employing dil aq $NaHSO_3$ in order to avoid debromination of **6**, which was isolated as a syrup. After recrystallization from MeOH, **6** (97 mg, 47%) had mp 114–116°C; $[\alpha]_D$ + 16.7° (*c* 1, $CHCl_3$); MS *m*/*z* (relative intensity %): 501 (1.0), 458, 460 (1.2), 403 (1.1), 336, 338 (8.1), 187, 189 (1.1), 122 (49.8), 105 (100). Anal. Calcd for $C_{35}H_{26}Br_2O_{10}$: C, 54.85; H, 3.42. Found: C, 55.20; H, 3.85.

*2-Propyl 6-*O-*acetyl-3-bromo-3,4-dideoxy-α-*D-glycero-*hex-3-enopyranosid-2-ulose* (**8**).—To a solution of 2-propyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**7**, 0.08 g, 0.3 mmol) in dry CH_2Cl_2, bromine was added dropwise at 0°C in the dark. The bromine decolorization was rapid at the beginning of the addition, and then the red color remained. After 30 min a spot with R_f 0.53, and no starting material, was detected by TLC (2:1 hexane–EtOAc). The mixture was diluted with CH_2Cl_2 (50 mL) and treated as described previously for other brominations. The resulting syrup was purified by column chromatography (4:1 hexane–EtOAc) to afford compound **8** as a clear oil (0.07 g, 65%); it had $[\alpha]_D$ + 80° (*c* 1, $CHCl_3$); MS *m*/*z* (relative intensity %): 306, 308 (0.3), 247, 249 (5.5), 234, 236 (0.7), 218, 220 (2.7), 205, 207 (1.5), 187, 189 (4.9), 176, 178 (100), 97 (8.8), 89 (5.9), 68 (3.0), 43 (59.7). Anal. Calcd for $C_{11}H_{15}BrO_5$: C, 43.02; H, 4.92; Br, 26.02. Found: C, 42.88; H, 4.69; Br, 25.85.

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