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THE CONFORMATION OF 2,3,4-TRI-*O*-ACETYL-D-XYLONO-1,5-LACTONE

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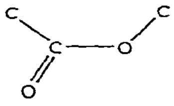
ABSTRACT

A conformational analysis of 2,3,4-tri-*O*-acetyl-D-xylono-1,5-lactone (**5**) has been performed by using ^{1}H-n.m.r. spectral data. Evidence is presented that the C-3 and C-4 acetoxyl groups are *anti*-periplanar. The possible contribution of attractive 1,3- and 1,4-interactions between the electropositive lactone-ring oxygen and the *endo*-acetoxyl groups at C-3 and C-4 to the conformational stability of **5** is discussed.

INTRODUCTION

The conformational characteristics of the lactone ring in δ-lactones is a subject of general interest. Information about the electron distribution in the lactone group of D-aldono-1,5-lactones and the conformational characteristics of the carbohydrate ring system are of significance in understanding the chemical[1–3] and biological[4–8] properties of these molecules.



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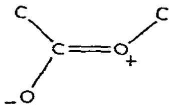

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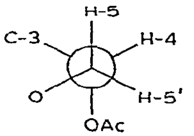

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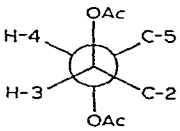

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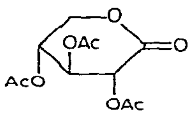

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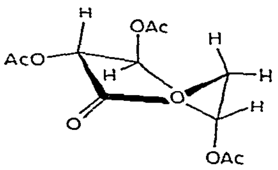

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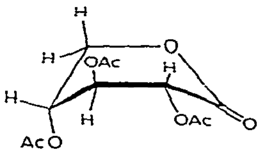

7 ($B_{1,4}$)

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Previous reports[9-14] on δ-lactones have suggested that molecular orbital delocalization in the lactone system **1** results in a decrease in the C=O bond-order and an increase in that of the C–O bond. An important consequence of such changes in bond order, shown by the resonance form **2**, is constraint of the five atoms composing the lactone functional group; as a result, the lactone ring is required to adopt either a half-chair or a boat conformation. It has been generally assumed that D-aldono-1,5-lactones adopt the half-chair conformation[1,4,15], although the conformation of D-glucono-1,5-lactone has been shown by X-ray crystallography to be a distorted chair[15,16]. In addition, the reported ^{1}H-n.m.r. spectroscopic analysis of 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*arabino*-hexono-1,5-lactone suggests a distorted boat conformation for this molecule[17]. We now report a study by ^{1}H-n.m.r. spectroscopy of the conformation of 2,3,4-tri-*O*-acetyl-D-xylono-1,5-lactone (**5**).

RESULTS AND DISCUSSION

Deductions about the conformation of the lactone ring in **5** are based on considerations of the geminal, vicinal, and long-range coupling constants given in Table I. The signal for H-2 appeared as a doublet at lowest field with $J_{2,3}$ 8.6–8.9 Hz. The magnitude of $J_{2,3}$ indicates an approximately *anti*-periplanar orientation of H-2/H-3. The small values found for the vicinal couplings $J_{3,4}$ = 2.5, $J_{4,5}$ = 2.2, and $J_{4,5'}$ = 2.7 Hz, however, are characteristic of ring hydrogens having approximately *gauche*-orientations.

TABLE I

N.M R. DATA[a] FOR 2,3,4-TRI-*O*-ACETYL-D-XYLONO-1,5-LACTONE (5)

Solvent	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*	*OAc*
$CDCl_3$	4.49 d[a] $J_{2,3} = 8\ 6$	4.72—— [b]	——4.94[b] m	5 42 dd $J_{4,5} = 2\ 2$ $J_{5,5'} = -13.2$[c]	5.61 dq $J_{1,5'} = 2\ 7$ $J_{3,5'} = 1\ 2$ $J_{5,5'} = -13.2$	7.80–7 95
C_6D_6	4 52 d $J_{2\ 3} = 8.9$	4 71 dd $J_{2\ 3} = 8\ 9$ $J_{3\ 4} = 2\ 5$	5.16 m [b]	6 10—— [b]	——6 25[b]	8 15–8.55

[a]Chemical shifts (τ values) and 1st-order coupling constants (Hz), signal multiplicities are indicated by: d, doublet; dd, double doublet; m, complex multiplet; dq, double quartet. [b]Complex multiplet not analyzed on a first-order basis [c]The sign of J_{gem} is assumed to be negative[18].

The magnitude of a geminal coupling often yields valuable information about the orientation of an electron-withdrawing group on an adjacent carbon atom[19, 20]. For **5**, the magnitude (—13.2 Hz) of $J_{5,5'}$ indicates that AcO-4 has an *endo* orientation and an *anti*-periplanar relationship with one of the C-5 hydrogens, as illustrated by the Newman projection **3**. The $J_{4,5}$ and $J_{4,5'}$ values (Table I) clearly indicate *gauche*-orientations for H-4/H-5 and H-4/H-5′, and are consistent with the approximate representation of the C-4/C-5 fragment in **5** as **3**.

Unfortunately, the $J_{3,4}$ value of 2.5 Hz does not permit an unequivocal decision as to the nature of the H-3/H-4 relationship. However, the magnitude of the long-range coupling $J_{3,5'}$ = 1.2 Hz indicates that H-3 and H-5′ have an approximately planar W configuration; thus, H-3 has an *exo*-orientation[19,20]. Since **5** has the D-*xylo* stereochemistry, and the orientation about the C-4/C-5 fragment is that shown by **3**, then the *exo*-orientation indicated for H-3 allows the *anti*-periplanar relationship between the C-3 and C-4 acetoxyl groups shown in **4** to be deduced.

Of the possible half-chair and boat conformations for **5**, only the $B_{1,4}$ conformation (**7**) is consistent with projection formulae **3** and **4**. However, **7** lacks the desired planarity of the five atoms composing the lactone group, and the $J_{2,3}$ value for **5** (Table I) cannot be interpreted in terms of a $B_{1,4}$ conformation where the dihedral angle H-2–C-2/C-3–H-3 would be ~120°.

Examination of a Dreiding model of **5** indicates that, in the $B_{1,4}$ conformation, there would be a non-bonded 1,3-interaction between the *endo*-acetoxyl group at C-3 and H-5 (*endo*), and an eclipsing interaction between the lactone carbonyl group and the *exo*-acetoxyl group at C-2. Distortions of bond angles have often been suggested to take place in cyclic molecules, in order to minimize steric and non-bonded interactions. For **5** in the $B_{1,4}$ conformation, twisting about the C-2/C-3 bond would minimize the non-bonded interaction between the *endo*-acetoxyl group at C-3 and H-5 (*endo*), and increase the H-2–C-2/C-3–H-3 dihedral angle. Twisting about the C-1/C-2 bond would relieve the eclipsing interaction of the lactone carbonyl group with the *exo*-acetoxyl group at C-2, and also produce an approximately planar lactone group.

For **5**, conformation **6** best accommodates the stereochemistry indicated by the ^{1}H-n.m.r. spectral data, minimizes steric and non-bonding interactions, and contains an approximately planar lactone group. X-Ray analysis of carbohydrate lactones[16, 21] suggests that, in the solid state, the lactone group is slightly distorted; hence, it is perhaps reasonable to assume that a slight distortion of the lactone group can also occur in **5**.

TABLE II

APPROXIMATE PROTON–PROTON DIHEDRAL ANGLES (ϕ) FOR 2,3,4-TRI-*O*-ACETYL-D-XYLONO-1,5-LACTONE (5)

Angles	*Calculated*[a] *(degrees)*	*Observed*[b] *(degrees)*
$\phi_{2,3}$	165–169	153
$\phi_{3,4}$	54	49
$\phi_{4,5}$	56	63
$\phi_{4,5'}$	53	57

[a]Calculated from coupling constants (J) in Table I [b]Approximate values measured from a Dreiding model

Assuming a Karplus-type dependence of coupling constants, the approximate dihedral angles for **5** were estimated from J values[22,23] (Table I), and compared to the dihedral angles measured from a Dreiding model of **6** (Table II). Although such calculations and measurements make no allowances for angle strain and the dependence of coupling constants on the conformational relationship between protons and electronegative substituents[22], the agreement between the calculated and measured values is quite good and serves as a further indication that the conformation of the lactone ring in **5** is best approximated by conformation **6**.

Conformation **6** is interesting, because it contains two *endo*-acetoxyl groups. Previous studies of the conformational characteristics of pentopyranose derivatives indicate that *endo*-substituent groups have less of a destabilizing effect on the conformation than steric considerations alone would suggest[24,25]. The conformational preference exhibited by an electronegative substituent on a six-membered ring is strongly dependent upon the nature of other ring atoms, especially those which have a 1,3- or 1,4-relationship to the electronegative substituent. An electrostatic interaction between a polar acetoxyl group and a cross-ring heteroatom or electron-attracting group is expected to make an important contribution to the conformational energy of the molecule, and the conformer having the acetoxyl group *endo* is preferred[25,26]. For compound **5**, conformation **6** could be substantially stabilized by attractive 1,3- and 1,4-interactions between the electropositive lactone ring oxygen (see **2**) and the *endo*-acetoxyl groups at C-3 and C-4. Such interactions would be less likely to occur in D-glucono-1,5-lactone and 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*arabino*-hexono-1,5-lactone, since such conformations as **6** would introduce non-bonded 1,3- or 1,4-interactions between the bulky *endo*-hydroxymethyl group in the former, or -benzoyloxymethyl group in the latter, and the *endo*-substituents at C-3 or C-2, respectively.

The results presented here regarding the conformational characteristics of **5** are of interest with regard to previous studies concerning the stability of carbohydrate lactone rings[1–3,15,27,28]. In general, aldono-1,5-lactones are more labile than the aldono-1,4-lactones, and the rate of hydrolysis is affected by the nature and configuration of substituents[15,27,28]. The greater stability of the aldono-1,4-lactones has been attributed to the well-established fact that an *exo*-double-bond stabilizes a 5-membered ring and destabilizes a 6-membered ring[29]. However, 2,3,4-tri-*O*-methyl-D-xylono-1,5-lactone is more stable than the corresponding 1,4-lactone[15,27,28]. This may indicate a lower ground-state free-energy for the 1,5-lactone, although it is possible that the greater stability of the 1,5-lactone is, in part, associated with a larger transition-state free-energy difference for its hydrolysis compared with that of the 1,4-lactone[2,15,29]. It is tempting to suggest that the 1,5-lactone may have a conformation similar to that of the triacetate **5**, and to suggest that attractive 1,3- and 1,4-interactions between *endo*-methoxyl groups at C-3 and C-4 and the polarized lactone-ring oxygen could account for the greater stability of the 1,5-lactone compared with the 1,4-lactone. However, further work is necessary to establish definitely such a relationship.

EXPERIMENTAL

General methods.—^{1}H-N.m.r. spectra were recorded for 10% solutions (internal Me_4Si) with a Varian HA 100 spectrometer; chemical shifts are reported on the τ scale, and coupling constants (J) in Hz. Assignments were substantiated by double-irradiation experiments. Mass spectra were obtained on an AEI MS-1201 spectrometer with direct sample introduction; data are reported in the form m/e (percent base-peak intensity).

Organic solvents were dried over anhydrous magnesium sulfate, and solutions were concentrated at reduced pressure on a rotary evaporator at <60° (bath).

2,3,4-Tri-O-acetyl-D-xylono-1,5-lactone (5). — 2,3,4-Tri-*O*-acetyl-D-xylopyranose[30] (1.0 g) was slowly added to a magnetically stirred solution of chromium trioxide (3 g) in glacial acetic acid (30 ml). After 10 min at room temperature, the reaction solution was diluted with chloroform (70 ml) and washed with ice-cold water (9 × 50 ml). The organic layer was dried, treated with activated carbon, and concentrated to give 5 as a colorless syrup (0.81 g, 82%), $[\alpha]_D$ −63.4° (c 4, chloroform). Compound 5 is levorotatory, as expected[31] for a D-xylono-1,5-lactone. The ^{1}H-n.m.r. spectral data are given in Table I. Mass spectrum: m/e 274 (M^+, 7%), 232 (40), 214 (7), 172 (34), 171 (77), 157 (26), 145 (51), 131 (13), 130 (51), 129 (23), 128 (63), 115 (77), 113 (23), 112 (11), 103 (100), 87 (20), 86 (31), 84 (19), 73 (20), 60 (31), and 43 (100).

Conversion of 5 *into 2,4-di-O-acetyl-3-deoxy*-D-glycero-*hex-2-enono-1,5-lactone.* — To a solution of 2,3,4-tri-*O*-acetyl-D-xylono-1,5-lactone (5, 118 mg) in anhydrous dichloromethane (10 ml) at 0° triethylamine (0.5 ml) was added. The mixture was kept in a stoppered flask at 0° for 16 h, and then extracted with ice-cold aqueous HCl. The organic layer was dried, treated with activated carbon, and concentrated to give the title compound as a light-yellow syrup (72 mg, 82%), $[\alpha]_D$ +141° (c 0.7, chloroform); lit.[32] $[\alpha]_D$ +139.9°. ^{1}H-N.m.r. data ($CDCl_3$): τ 3.46 (dd, 1 H, $J_{3,4}$ 5.9, $J_{3,5'}$ 1.2 Hz, H-3), 4.57 (m, 1 H, H-4), 5.38 (dd, 1 H, $J_{4,5}$ 3.2, $J_{5,5'}$ −12.9 Hz, H-5), 5.48 (dq, 1 H, $J_{4,5'}$ 2.8, $J_{3,5'}$ 1.2, $J_{5,5'}$ −12.9 Hz, H-5'), 7.78 (s, 3 H, enol AcO), and 7.93 (s, 3 H, AcO). Mass spectrum: m/e 214 (M^+, 1%), 172 (100), 155 (39), 154 (13), 130 (78), 126 (10), 113 (94), 85 (100), 69 (70), 44 (100), and 43 (75).

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REFERENCES

1 Y. Pocker and E. Green, *J. Am. Chem. Soc.*, 95 (1973) 113–119
2 Y. Pocker and E. Green, *J. Am. Chem Soc.*, 96 (1974) 166–173.
3 Y. Pocker and E. Green, *J. Am. Chem. Soc.*, 98 (1976) 6197–6202.

4 D. H. Leaback, *Biochem. Biophys. Res. Commun.*, 32 (1968) 1025–1030.
5 Y. C. Lee, *Biochem. Biophys. Res. Commun.*, 35 (1969) 161–167.
6 E. T. Reese, F. W. Parrish, and M. Ettlinger, *Carbohydr. Res.*, 18 (1971) 381–388.
7 M. Pokorny, *Acta Bot. Croat.*, 33 (1974) 111–116.
8 H. W. Diehl, M. Pokorny, E. Zissis, R. K. Ness, and H. G. Fletcher, Jr., *Carbohydr. Res.*, 38 (1974) 364–368.
9 J. F. McConnell, A. McL. Mathieson, and B P. Schoenborn, *Tetrahedron Lett.*, (1962) 445–448.
10 A. McL. Mathieson, *Tetrahedron Lett.*, (1963) 81–84.
11 K. K. Chenng, K. H Overton, and G. A. Sim, *Chem. Commun.*, (1965) 634–635.
12 R. C. Sheppard and S. Turner, *Chem. Commun.*, (1968) 77–78.
13 F. I. Carroll, G. N. Mitchell, J. T. Blackwell, A. Sobti, and R. Meck, *J. Org. Chem.*, 39 (1974) 3890–3896.
14 C. A. L. Filgueiras and J. E. Huheey, *J. Org. Chem.*, 41 (1976) 49–53
15 J. F. Stoddart, *Stereochemistry of Carbohydrates*, Wiley–Interscience, New York, 1971, pp. 177–186.
16 M. L. Hacket and R. A. Jacobson, *Chem. Commun*, (1969) 1179.
17 R. M. de Lederkremer, M. I. Litter, and L F. Sala, *Carbohydr. Res.*, 36 (1974) 185–187.
18 L. D. Hall and J. F. Manville, *Carbohydr. Res.*, 4 (1967) 271–273.
19 P. L. Durette and D. Horton, *Adv. Carbohydr. Chem. Biochem.*, 26 (1971) 49–125.
20 P. L. Durette, D. Horton, and J. D. Wander, *Adv. Chem. Ser.*, 117 (1973) 147–176.
21 M. E. Gress and G. A. Jeffrey, *Carbohydr. Res*, 50 (1976) 159–168.
22 L M Jackman and S. Sternhell, *Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, Elmsford, N.Y., 2nd edition, 1969.
23 B. Coxon, *Carbohydr. Res.*, 8 (1968) 125–134.
24 P. L. Durette and D. Horton, *Chem. Commun.*, (1970) 1608–1609.
25 P. L. Durette and D. Horton, *Carbohydr. Res*, 18 (1971) 57–80.
26 F. A. Carey, P. M Smith, R J. Maher, and R. F. Bryan, *J. Org. Chem*, 42 (1977) 961–967.
27 H. D. K. Drew, E. H. Goodyear, and W. N. Haworth, *J. Chem. Soc.*, (1927) 1237–1245.
28 S. R. Carter, W. N. Haworth, and R. A. Robinson, *J. Chem. Soc*, (1930) 2125–2133.
29 H C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, 76 (1954) 467–474.
30 C. S. Hudson and J. K. Dale, *J. Am Chem. Soc.*, 40 (1918) 997–1001.
31 H. S. Isbell and C. S. Hudson, *Bur. Stand. J. Res*, 8 (1932) 327–338.
32 D. M. Mackie and A. S. Perlin, *Carbohydr. Res*, 24 (1972) 67–85.