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THE CRYSTAL STRUCTURE OF ETHYL 2,3-DIDEOXY-α-D-*erythro*-HEX-2-ENOPYRANOSIDE

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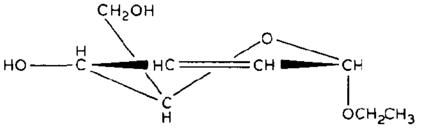
ABSTRACT

The crystal structure of ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside, $C_8H_{14}O_4$, is orthorhombic, $P2_12_12_1$, with cell dimensions at 123 K [293 K] a = 11.220(2) [11.319(1)], b = 18.387(3) [18.458(2)], c = 8.509(2) [8.635(1)] Å, Z = 8. There are two symmetry-independent molecules in the asymmetric unit. In both molecules, the conformation is $^{o}H_5$. The alkenic bond is almost exactly planar in one molecule, with C-1–C-2–C-3–C-4 = +0.8°. In the other molecule, this torsion angle is +3.7°. The glycosidic torsion angle, O-5–C-1–O-1–C-7, has normal *exo*-anomeric values of +71 and +64°. The conformation of the ethoxyl group is extended, with C-1–O-1–C-7–C-8 = +162 and +170°. The primary alcohol group has different orientations, *g*/*t* on one molecule, *g*/*g* on the other. The characteristic glycosidic bond-shortening observed in the pyranosides is modified in this enopyranoside. Both the ring bond, O-5–C-1, and the glycosidic bond, C-1–O-1, are short, with distances ranging from 1.409 to 1.425 Å. Solution and solid-state c.p.-m.a.s., ^{13}C-n.m.r. spectra are reported.

INTRODUCTION

In this study, we examined the geometrical effect of having an alkenic bond between C-2 and C-3 in a pyranoid ring. The molecule, ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside, would be expected to have the $^{o}H_5$ conformation, shown in 1, in which the alkenic carbon bonds are coplanar, and the primary alcohol group is equatorial. The alternative half-chair conformation, ^5H_o, which requires the primary alcohol group to be axial, would be expected to be the less stable conformer, as for pyranosides.



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The difference in torsion angles in the acetal moiety of an enopyranoside, with an $^{O}H_5$, and those of a pyranoside, with a $^{4}C_1$, conformation should result in a difference in anomeric energy, which depends on the relative orientations of the 2*p* orbital on C-1, and the O-1 and O-5, lone-pair orbitals[1]. Previous studies[2,3] suggested that this difference will be reflected in small, but significant, differences in the acetal C–O bond-lengths, which can be observed by crystal structure analysis.

This crystal structure is also interesting because it contains two symmetry-independent molecules, which may differ conformationally because of different crystal-field environments. The solid-state c.p.-m.a.s., ^{13}C-n.m.r. spectrum should, therefore, be resolvable into two separate spectra, one for each molecule.

EXPERIMENTAL

Excellent, diffraction-quality crystals were provided by Professor B. Fraser-Reid of Duke University. The crystal and intensity data were obtained on a CAD-4 diffractometer with CuKα radiation at 123 K. The structure was solved with the direct method program, MULTAN-78 (ref. 4), using the 240 largest E-values. The resulting E-map revealed two molecular fragments, each with 12 peaks, which were readily identified as the non-hydrogen atoms of the two symmetry-independent molecules. The 14 hydrogen atoms associated with each molecule were located on difference maps. The structure was refined by QWKREF (ref. 5), a full-matrix, least-squares program, with anisotropic temperature-factors for the non-hydrogen atoms and isotropic temperature-factors for the hydrogen atoms. The crystal data, details of the intensity-data collection and of the refinement procedures, are given

TABLE I

CRYSTAL DATA, INTENSITY-MEASUREMENT DATA, AND PARAMETER-REFINEMENT DATA FOR ETHYL 2,3-DIDEOXY-α-D-*erythro*-HEX-2-ENOPYRANOSIDE

$C_8H_{14}O_4$; mol.wt. = 174.20; m.p. = 371 K; $P2_12_12_1$; Z = 8

Cell dimensions at 123 K [293 K]: a = 11.220(2) [11.319(1)], b = 18.387(3) [18.458(2)], c = 8.509(2) [8.635(1)]

$D_x = 1.283$ g · cm^{-3}, $D_m = 1.274$ g · cm^{-3}

Crystal dimensions: 0.25 × 0.40 × 0.47 mm

Radiation: CuKα (λ = 1.54178 Å) with Ni filter; $\mu_{CuK\alpha} = 8.718$ cm^{-1}

Absorption correction applied, using program ABL[a]; no correction for extinction (reflection 310 omitted)

Cell dimensions based on 36 reflections, with $34.9° \leq \theta \leq 44.0°$

2078 intensities measured by $\omega/2\theta$ scan, of which 2076 were unique, and 1992 had $F_{obs} \geq 3\sigma(F_{obs})$

Function minimized, $R = \Sigma w(|F_o| - |kF_c|)^2$, using program QWKREF[b], where $w = \sigma^{-2}(F_o)$ was based on counting statistics

Final agreement-factors: R = 0.029, R_w = 0.030, s = 1.89.

[a] Ref. 6. [b] Ref. 5.

TABLE II

ATOMIC PARAMETERS[a] FOR THE CRYSTAL STRUCTURE OF ETHYL 2,3-DIDEOXY-α-D-*erythro*-HEX-2-ENOPYRANOSIDE AT 123 K

Atom	*Molecule A*				*Molecule B*			
	Fractional coordinates[b]			B_{eq} *or* B[c]	*Fractional coordinates*[b]			B_{eq} *or* B[c]
	x	y	z		x	y	z	
C-1	3779(1)	4020(1)	6332(2)	146(3)	1832(2)	1633(1)	1586(2)	187(3)
C-2	3958(2)	4483(1)	7764(2)	172(3)	1851(2)	1409(1)	−107(3)	210(4)
C-3	4386(2)	5151(1)	7676(2)	169(3)	2411(2)	1795(1)	−1187(3)	205(3)
C-4	4712(1)	5501(1)	6141(2)	146(3)	3128(2)	2459(1)	−791(2)	163(3)
C-5	4131(1)	5093(1)	4770(2)	128(3)	3396(1)	2461(1)	973(2)	144(3)
C-6	4727(2)	5294(1)	3241(2)	157(3)	3915(1)	3162(1)	1571(2)	154(3)
C-7	2205(2)	3311(1)	5164(2)	190(3)	2370(2)	1205(1)	4118(3)	236(4)
C-8	948(2)	3079(1)	5527(3)	227(4)	2872(2)	540(1)	4908(3)	234(4)
O-1	2528(1)	3900(1)	6204(1)	156(2)	2461(1)	1101(1)	2453(2)	198(2)
O-4	4395(1)	6254(1)	6099(2)	186(2)	4201(1)	2495(1)	−1692(2)	207(2)
O-5	4278(1)	4320(1)	4958(1)	145(2)	2308(1)	2338(1)	1818(2)	172(2)
O-6	4104(1)	5046(1)	1881(2)	160(2)	3078(1)	3739(1)	1345(2)	159(2)
H-1	419(2)	356(1)	646(2)	16(4)	100(2)	167(1)	201(2)	12(4)
H-2	377(2)	427(1)	870(3)	22(5)	140(2)	99(1)	−37(2)	18(4)
H-3	453(2)	543(1)	860(3)	18(4)	238(2)	168(1)	−227(3)	18(4)
H-4	559(2)	550(1)	603(2)	17(4)	266(2)	291(1)	−107(2)	12(4)
H-O-4	367(2)	628(1)	625(3)	25(5)	463(2)	212(1)	−145(3)	32(5)
H-5	328(2)	521(1)	472(2)	6(3)	398(2)	206(1)	124(2)	9(3)
H1-6	551(2)	506(1)	320(2)	13(4)	470(2)	327(1)	99(2)	18(4)
H2-6	480(2)	583(1)	322(2)	14(4)	415(2)	311(1)	272(3)	16(4)
H-O-6	354(2)	535(1)	167(3)	29(5)	342(2)	413(1)	159(3)	30(5)
H1-7	229(2)	348(1)	411(3)	16(4)	286(2)	164(1)	439(3)	20(4)
H2-7	280(2)	289(1)	532(3)	22(5)	151(2)	128(1)	443(3)	24(5)
H1-8	90(2)	290(1)	660(3)	34(5)	371(2)	47(1)	460(3)	21(4)
H2-8	70(2)	268(1)	480(3)	35(5)	239(2)	12(1)	459(3)	30(5)
H3-8	35(2)	347(1)	534(3)	31(5)	282(2)	60(1)	604(3)	25(5)

[a]E.s.d. values given in parentheses refer to the least significant digit. [b]Fractional coordinates × 10^4 for non-hydrogen atoms, × 10^3 for hydrogen atoms. [c]B_{eq} × 10^2 (in Å^2) for non-hydrogen atoms, calculated from the refined, anisotropic, thermal parameters; B × 10 (in Å^2) for hydrogen atoms, refined, isotropic, thermal parameters.

in Table I. The atomic notation and thermal ellipsoids[7] are shown in Fig. 1. Atomic positional and thermal parameters* are given in Table II.

DESCRIPTION OF THE MOLECULAR STRUCTURE

The conformation of the two symmetry-independent molecules is shown in

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*Lists of structure factors and anisotropic thermal parameters are deposited with, and can be obtained from Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands, Reference should be made to No. BBA/DD/276/*Carbohydr. Res.*, 128 (1984) 1–10.

Fig. 1. The molecular dimensions, *i.e.*, bond lengths, valence angles, and principal torsion-angles, are given in Table III. Both molecules have the $^{\circ}H_5$ conformation, with similar puckering parameters[8]; for molecule A, $Q = 0.44$ Å, $\theta = 51°$, $\varphi = 318°$; for molecule B, $Q = 0.50$ Å, $\theta = 53°$, $\varphi = 320°$. These are close to the values of $\theta = 51°$, $\varphi = 330°$ for the ideal $^{\circ}H_5$ conformation, in which the O-5 and C-5 displacements are equal, "above" and "below" the mean plane of the ring. This is the anticipated, stable conformation for a molecule having a planar, or almost planar, C-2=C-3 alkenic bond and an equatorial orientation of the primary alcohol group.

The alkenic bond C-2=C-3 is the more exactly planar in A, with C-1–C-2–C-3–C-4 = +0.8°, as compared with +3.7° in B. The largest differences in the ring torsion-angles between molecules is in the region of the ring-oxygen atom, with C-4–C-5–O-5–C-1 = +60° and +67° for A and B, respectively. The glycosidic torsion-angles comply with the favored, *exo*-anomeric orientation, with O-5–C-1–O-2–C-7 angles of +71° and +64°. The ethoxyl group is extended, with C-1–O-1–C-7–C-8 = +162° and +170°. The primary alcohol group has different orientations in the two molecules, being *gauche*/*trans* on A, and *gauche*/*gauche* on B. These are the two permitted orientations that avoid the "peri" interaction with the equatorial hydroxyl group on C-4.

With the exception of bonds in the acetal moiety, the bond lengths in the two molecules differ by 0.001 to 0.005 Å (less than 3σ), with the bonds in A tending to be longer than those in B. These small differences are associated with the difference in thermal motion of the two molecules, discussed later. The larger differences (not accountable to thermal motion) in the O-5–C-1–O-1–C-7 acetal sequence of bonds are ΔA − B: −0.007(2), +0.011(2), +0.012(2) Å. In both molecules, C-1–O-1 is shorter than O-1–C-7, namely, by 0.020(2) Å in A and by 0.019(2) Å in B. An unusual feature of the crystal structure is that the glycosidic oxygen atom, O-1, is the acceptor of a strong hydrogen-bond (H · · · O = 1.766 Å) in molecule A, but no hydrogen bond in molecule B. In the majority of pyranoside crystal structures, the glycosidic oxygen atoms are either not hydrogen-bonded or accept very weak hydrogen-bonds (H · · · O $\gtrsim$ 2.0 Å)[9].

THERMAL-MOTION ANALYSIS

The isotropic equivalent, atomic temperature-factors, B_{eq}, given in Table II, show that molecule B has greater thermal motion than molecule A. This is a consequence of the intermolecular forces discussed later. To analyze this unusual feature, which could be relevant to a subsequent, solid-state, n.m.r. study, a rigid-body analysis was carried out[10]. The results are given in Table IV. Good least-squares fits are obtained that are comparable to those found in other monosaccharide crystal-structures[11–13]. The $\langle \mathrm{rms}|U_{ij}^{\mathrm{exp}} - U_{ij}^{\mathrm{calc}}|\rangle$ values, taking the six ring-atoms as a rigid body, were 0.0007(10) Å for both molecules A and B. The ring bond-lengths, corrected by LIBCOR[14] for thermal-motion foreshortening, are

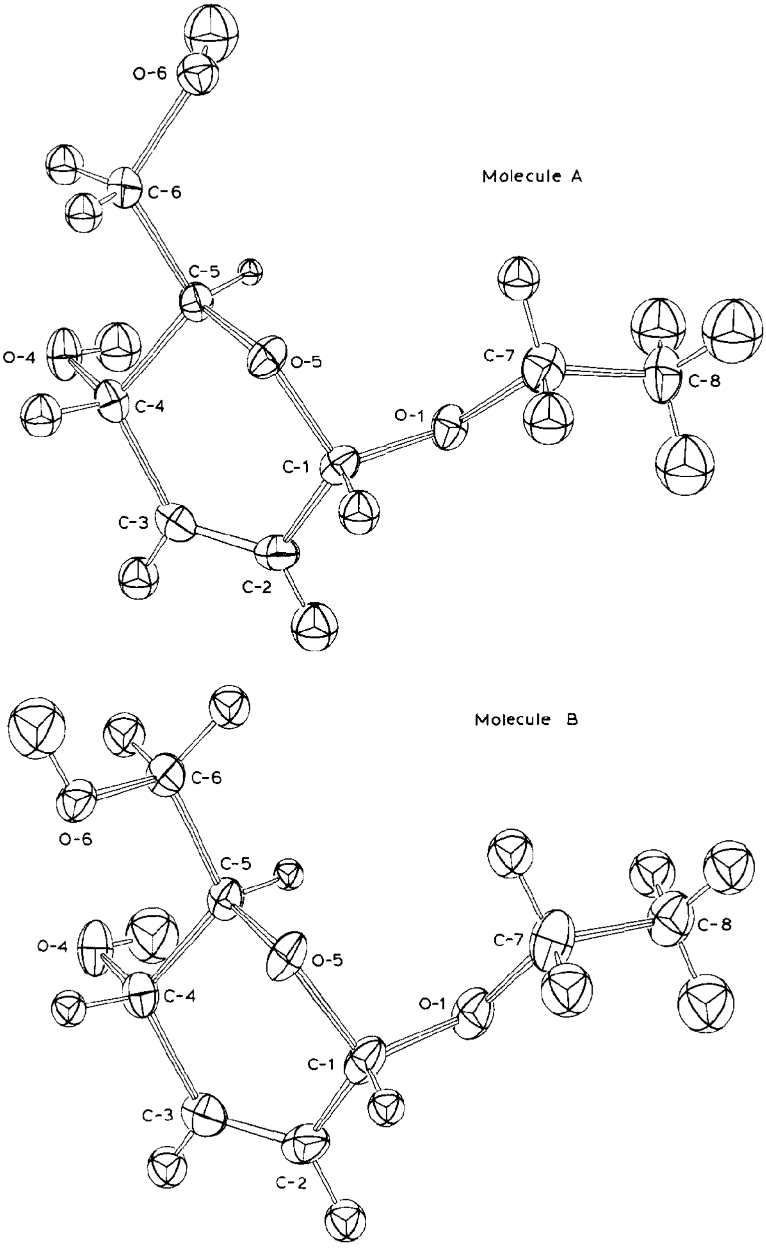

Fig. 1. Atomic notation and thermal ellipsoids at 50% probability for molecules A and B of ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside.

TABLE III

MOLECULAR DIMENSIONS[a] OF ETHYL 2,3-DIDEOXY-α-D-*erythro*-HEX-2-ENOPYRANOSIDE AT 123 K

Parameter	*Molecule A*	*Molecule B*
Bonds		
C-1–C-2	1.500(2) [1.506]	1.499(3) [1.506]
C-2–C-3	1.322(3) [1.324]	1.320(3) [1.325]
C-3–C-4	1.501(3) [1.506]	1.501(3) [1.506]
C-4–C-5	1.533(2) [1.538]	1.531(2) [1.538]
C-5–O-5	1.439(2) [1.444]	1.435(2) [1.441]
O-5–C-1	1.409(2) [1.413]	1.416(2) [1.421]
C-1–O-1	1.425(2)	1.414(2)
C-4–O-4	1.430(2)	1.429(2)
C-5–C-6	1.509(2)	1.504(2)
C-6–O-6	1.427(2)	1.428(2)
O-1–C-7	1.445(2)	1.433(2)
C-7–C-8	1.506(3)	1.505(3)
Valence angles		
C-1–C-2–C-3	122.0(2)	121.9(2)
C-2–C-3–C-4	122.5(2)	122.4(2)
C-3–C-4–C-5	110.4(1)	109.1(1)
C-4–C-5–O-5	110.5(1)	108.9(1)
C-5–O-5–C-1	115.7(1)	113.3(1)
O-5–C-1–C-2	113.5(1)	112.3(2)
O-5–C-1–O-1	112.9(1)	111.9(1)
C-2–C-1–O-1	106.4(1)	107.7(1)
C-3–C-4–O-4	112.1(1)	111.6(1)
C-5–C-4–O-4	110.4(1)	111.1(1)
C-4–C-5–C-6	110.4(1)	114.2(1)
O-5–C-5–C-6	106.7(1)	107.1(1)
C-5–C-6–O-6	113.8(1)	109.7(1)
C-1–O-1–C-7	114.2(1)	112.8(1)
O-1–C-7–C-8	108.7(1)	107.8(2)
Torsion angles		
C-1–C-2–C-3–C-4	+0.8(3)	+3.7(3)
C-2–C-3–C-4–C-5	+17.6(2)	+16.9(2)
C-3–C-4–C-5–O-5	−45.6(2)	−49.8(2)
C-4–C-5–O-5–C-1	+59.9(2)	+67.0(2)
C-5–O-5–C-1–C-2	−40.6(2)	−45.0(2)
O-5–C-1–C-2–C-3	+9.3(2)	+9.0(3)
C-5–O-5–C-1–O-1	+80.5(2)	+76.3(2)
O-5–C-1–O-1–C-7	+71.0(2)	+63.8(2)
C-1–O-1–C-7–C-8	+161.6(1)	+169.8(2)
C-2–C-3–C-4–O-4	+141.2(2)	+140.0(2)
C-3–C-4–C-5–C-6	−163.4(1)	−169.5(1)
C-4–C-5–C-6–O-6	−168.9(1)	+62.4(2)
O-5–C-5–C-6–O-6	+71.0(2)	−58.2(2)

[a] Bond lengths in Å, valence and torsion angles in degrees. E.s.d. values given in parentheses refer to the least significant digit. Values in brackets are corrected for thermal motion, taking the six ring-atoms as a rigid body.

TABLE IV

RIGID-BODY, THERMAL-MOTION ANALYSIS[a]

Parameter	*Molecule A*				*Molecule B*			
T tensor[b]	137(23)		6(6)	−12(10)	140(11)		32(9)	1(8)
			156(10)	17(7)			122(9)	23(7)
				167(8)				261(6)
ω tensor[b]	8(1)		4(2)	−2(1)	12(3)		6(2)	−2(1)
			16(6)	−2(1)			19(3)	−2(1)
				12(6)				15(4)
	R.m.s. values	*a*	*b*	*c*	*R.m.s. values*	*a*	*b*	*c*
Principal axes of T[c]	0.13	81.3	123.1	145.5	0.16	92.8	99.9	169.7
	0.12	54.9	43.6	112.5	0.13	144.0	125.0	82.7
	0.11	35.6	113.2	64.6	0.10	126.0	36.5	95.7
Principal axes of ω[c]	4.4	67.4	32.9	112.6	4.9	60.4	34.7	106.4
	3.3	90.6	65.8	24.2	3.7	85.8	70.0	20.5
	2.4	22.3	110.2	80.9	2.9	29.4	117.6	80.8

[a] E.s.d. values in parentheses. Calculations based on six ring-atoms as a rigid body. [b] Tensors referred to crystal axes. In T, elements in $Å^2 \times 10^4$. In ω, elements in deg^2. [c] Axis directions in degrees, relative to crystal axes. For T, r.m.s. values in Å. For ω, r.m.s. values in degrees.

given in brackets in Table III. The mean bond-correction was 0.0045 Å for molecule A and 0.0058 Å for molecule B, thereby accounting for the small, but systematic, differences noted in the uncorrected values.

HYDROGEN BONDING

The hydrogen bonding consists of five-link, finite chains that are initiated with O-4-B–H and terminated in the glycosidic oxygen atom O-1-A. This pattern is similar to type II in a systematic analysis of carbohydrate hydrogen-bonding[9]. The ring-oxygen atoms of both molecules and the glycosidic oxygen atom of molecule B are not involved in hydrogen bonding. In the finite chain, shown diagrammatically in Fig. 2, O-4-A and O-1-A are in the same molecule as O-6-A of an adjacent chain. There are no bifurcated interactions.

Molecule A is the more rigidly hydrogen-bonded, with five donor or acceptor functions involving both ends of the molecule, whereas molecule B is only hydrogen-bonded with three donor or acceptor functions at O-4 and O-6. This is consistent with the observed difference in the rigid-body, thermal motion of the two molecules already described. The hydrogen bonds stabilize a helical core of A

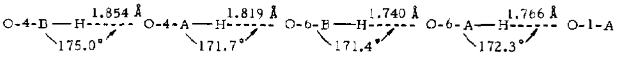

Fig. 2. Pattern of hydrogen bonding, with distances and angles calculated from corrected hydrogen-positions after normalization of O–H bond lengths to a mean, neutron-diffraction value of 0.97 Å.

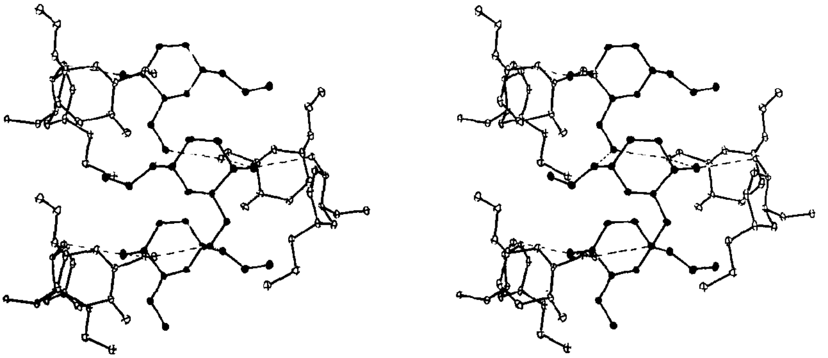

Fig. 3. Stereoview of A (shaded) and B (unshaded) molecules, with thermal ellipsoids at 30% probability. (Hydrogen bonds are dashed. The c axis is vertical.)

molecules, surrounded by B molecules interconnecting cores of A's. This is illustrated in the stereoview[7] of the crystal structure shown in Fig. 3.

N.M.R. SPECTROSCOPY

The solid-state and solution ^{13}C-n.m.r. spectra shown in Fig. 4 were provided by Dr. William Earl of the Los Alamos National Laboratory. The solid-state c.p.-m.a.s. spectrum was obtained, with high-power proton-decoupling, with a Bruker CXP-200 spectrometer, operated at a resonance frequency for ^{13}C of 50.3 MHz

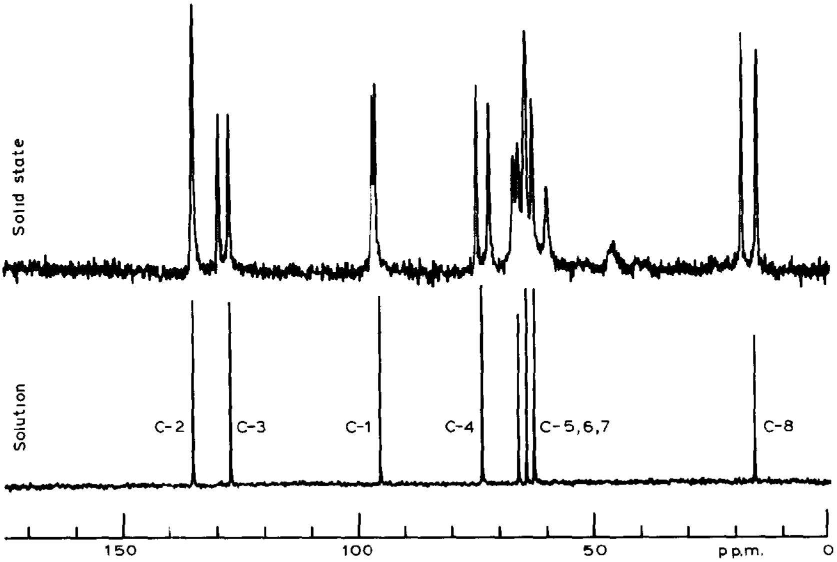

Fig. 4. Solid-state and solution ^{13}C-n.m.r. spectra of ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside, with atomic assignments for the solution spectrum corresponding to the notation of Fig. 1. (Chemical shifts are reported relative to tetramethylsilane.)

and magic-angle spinning at 4 kHz. The Hartmann–Hahn condition for cross polarization was met at 55 kHz. The spectrum is the accumulation of 6144 scans, each with 2-ms contact-time and 6.2-s pulse-delay. The solution spectrum is based on 4096 scans obtained, with 40° flip-angle, 1.5-s pulse-delay, and continuous, broadband proton-decoupling, with a Bruker WM-300 wide-bore spectrometer operated at a resonance frequency of 75.5 MHz for ^{13}C.

The solid-state spectrum is a "finger-print" of the crystalline material in the same sense as is an X-ray powder diffraction pattern, except that solid-state n.m.r. spectroscopy is sensitive to both the amorphous and crystalline states. Because the two enopyranoside molecules are so similar in structure, the differences in chemical shifts between corresponding carbon atoms in the two conformers are generally smaller than differences between different carbon atoms of one molecule.

The difference in chemical shifts for a particular carbon atom in one conformer *versus* the other is of the same magnitude as the difference in chemical shifts for a carbon atom in solution *versus* solid state. If this is a general observation, it will make difficult any distinction between chemical shifts arising from molecular conformation and those resulting from the intermolecular, crystal-field environment. A similar observation has been made[15] in comparison of the solution and solid-state, ^{13}C-n.m.r. spectra for α-D-glucose, α-D-glucose monohydrate, and β-D-glucose.

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