# The Solid-state and Solution Conformation of Some 1,2-*O*-Alkylidene Xylopyranoses. Application of Heteronuclear Long-range Coupling Constants to the Conformational Analysis of Dioxolane Rings

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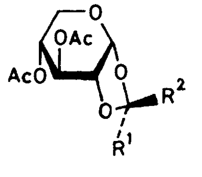
The molecular structures of 3,4-di-*O*-acetyl-1,2-*O*-[(*R*)-1-cyanoethylidene]-α-D-xylopyranose (**1**) and its (*S*)-isomer (**2**) have been determined from *X*-ray diffraction data. The pyranoid ring adopts a $^1C_4$ chair conformation for both compounds and the dioxolane ring presents $E_1$ and $^2E$ distorted envelope conformations for (**1**) and (**2**) respectively. The solution conformation of (**1**) and (**2**), and the ethylidene analogues (**3**) and (**4**), have been determined by n.m.r. spectroscopy. Proton–proton coupling constants, variable-temperature and n.O.e. experiments, and molecular mechanics calculations indicate that the major conformation of the pyranoid ring can be described as $^1C_4$ for (**1**), $^oS_2$ for (**2**) and (**4**), and as an equilibrium among $^4C_1$, $^1C_4$, and $^oS_2$ forms for (**3**). Long-range carbon–proton coupling constants can be interpreted in terms of $E_1$ and $E_{O2}$ conformations for the dioxolane ring of (**1**) and (**2**) respectively.

The conformational tendency of six-membered rings fused to a dioxolane ring has been studied for several years.[1] N.m.r. and *X*-ray data have shown that the conformation of the pyranoid ring of 1,2-*O*-alkylidene-α-D-hexopyranose derivatives depends on the nature of the sugar, the configuration at C-2 of the dioxolane ring, and the nature of the substituents on the hydroxy groups.[1–3] The pyranoid ring of tri-*O*-acetyl-α-D-galactopyranose derivatives presents a flattened $^4C_1$ conformation while those of the corresponding α-D-allo- and α-D-gulo-pyranose derivatives show a skew-boat $^oS_2$ conformation.[2] In contrast, the conformation of the pyranoid ring of tri-*O*-acetyl-1,2-*O*-alkylidene-α-D-glucopyranose derivatives strongly depends on the configuration at C-2 of the dioxolane ring and a $^oS_2$ conformation has been proposed for the isomers in which the alkyl group at C-2 of the dioxolane ring is in the *endo*-orientation, and a $^4C_1$ conformation for those compounds in which this group is *exo*. In the pentopyranose series, only 3,4-di-*O*-acetyl-1,2-*O*-[(S)-1-cyanoethylidene]-α-D-ribopyranose has been studied.[4] The pyranoid ring of this compound in the solid state is in a $^1C_4$ conformation while the conformation in solution can be described as an equilibrium between $^oS_2$ and $^1C_4$ forms.



(1) $R^1 = CN$, $R^2 = CH_3$
(2) $R^1 = CH_3$, $R^2 = CN$
(3) $R^1 = H$, $R^2 = CH_3$
(4) $R^1 = CH_3$, $R^2 = H$

In order to rationalise these results and to evaluate the different factors which govern the conformational tendency of these carbohydrate derivatives, reliable experimental data on a series of different compounds are needed. We now report on the solid-state and solution conformation of 1,2-*O*-[(*R*)-1-cyanoethylidene]-α-D-xylopyranose (**1**), 3,4-di-*O*-acetyl-1,2-*O*-[(*S*)-1-cyanoethylidene]-α-D-xylopyranose (**2**), and the solution conformation of 3,4-di-*O*-acetyl-1,2-O-[(*S*)-ethylidene]-α-D-xylopyranose (**3**), and 3,4-di-*O*-acetyl 1,2-O-[(*R*)-ethylidene]-α-D-xylopyranose (**4**).

Perspective views of (**1**) and (**2**) are given in Figures 1 and 2. Torsion angles, bond distances and angles, and intramolecular contacts are shown in Tables 1—4. Fractional atomic coordinates are presented in Tables 5 and 6. The conformation of the dioxolane rings can be described as distorted envelopes at C(1) for (**1**), ($E_1$), and at C(2) for (**2**), ($^2E$). The pyranoid ring is in both cases in a chair-like $^1C_4$ conformation. Intramolecular contacts O(2)···O(4) of the same order of magnitude to those found in the absence of hydrogen bonds[5] are also observed. Table 7 shows the chiral description of both compounds using the configurational angles.[1]

The 300 MHz $^1H$ n.m.r. spectra of compounds (**1**)—(**4**) were analysed iteratively and the best computed values of chemical shifts and coupling constants are given in Table 8. Table 9 shows the values of the vicinal coupling constants to be expected for (**1**) and (**2**), calculated from the crystallographic proton torsion angles using the equation proposed by Altona.[6] The spectrum of (**1**) showed vicinal coupling constant values similar to those expected for a $^1C_4$ conformation of the pyranoid ring and a long-range $^4J_{3,5}$ which, according to molecular models, could be assigned to this conformation only. The spectra of all other compounds, with the exception of that of (**3**), showed a large and positive coupling $J_{2,4}$, indicative of a planar W arrangement of these protons which should be expected for both $^1C_4$ and $^oS_2$ conformations. Table 10 shows the temperature dependence of coupling constants for compounds (**1**) and (**2**) and Table 11 presents the $^{13}C$ chemical shifts and the best computed values of $^nJ_{C,H}$ for (**1**) and (**2**). As the temperature decreased, slight broadening of the signals and changes in the chemical shifts were observed, both in the $^1H$ and $^{13}C$ spectra, although no coalescence temperature was reached. At low temperature, the vicinal coupling for (**1**), but not for (**2**), came closer to those expected for a $^1C_4$ conformation of the pyranoid ring.

The above spectroscopic evidence seemed to indicate the existence of conformational equilibria in solution and, in order to obtain reliable data on the geometry of conformers which could occur in these equilibria, molecular mechanics calculations using the MM2-program[7] were carried out for com-

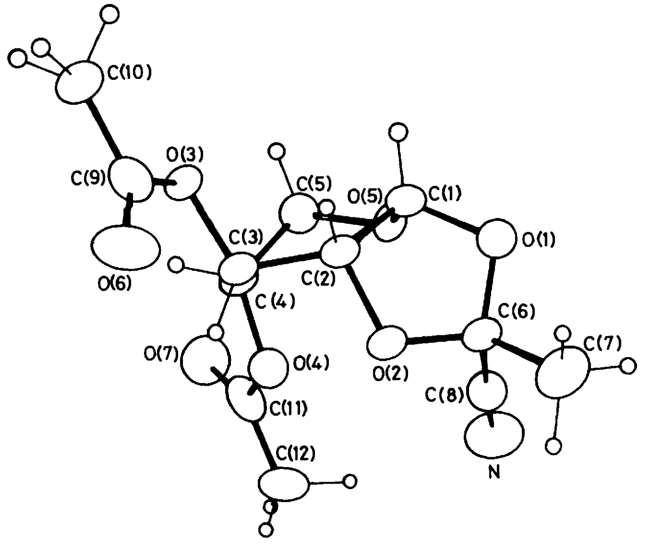


**Figure 1.** ORTEP[17] View of compound (**1**) showing the atomic numbering

**Table 1.** Selected torsion angles/° for compounds (**1**) and (**2**) from *X*-ray diffraction. E.s.d.s in parentheses

| Angle | (**1**) | (**2**) |
|---|---|---|
| O(5)–C(1)–C(2)–C(3) | –35.1(5) | –41.9(4) |
| C(1)–C(2)–C(3)–C(4) | 30.1(5) | 34.7(4) |
| C(2)–C(3)–C(4)–C(5) | –40.8(5) | –40.9(4) |
| C(3)–C(4)–C(5)–O(5) | 58.0(5) | 55.7(4) |
| C(4)–C(5)–O(5)–C(1) | –64.9(4) | –65.2(4) |
| C(5)–O(5)–C(1)–C(2) | 52.4(4) | 57.0(4) |
| O(1)–C(1)–C(2)–O(2) | –29.2(4) | –37.0(3) |
| C(1)–C(2)–O(2)–C(6) | 13.7(4) | 33.7(3) |
| C(2)–O(2)–C(6)–O(1) | 71(4) | –18.4(3) |
| O(2)–C(6)–O(1)–C(1) | –26.8(4) | –6.4(3) |
| C(6)–O(1)–C(1)–C(2) | 34.4(4) | 26.8(3) |
| H(1)–C(1)–C(2)–H(2) | –32.3(4) | –41.5(3) |
| H(2)–C(2)–C(3)–H(3) | –76.4(3) | –76.5(3) |
| H(3)–C(3)–C(4)–H(4) | 69.5(3) | 71.3(3) |
| H(4)–C(4)–C(5)–H(5A) | –68.3(4) | –65.5(4) |
| H(4)–C(4)–C(5)–H(5B) | 55.3(4) | 51.2(3) |

pounds (**1**) and (**2**). The three expected local minima corresponding to the $^{1}C_{4}$, $^{4}C_{1}$, and $^{o}S_{2}$ conformations were found with the relative[8] 'steric energies' shown in Table 12. The global minima occurred in both cases for the $^{1}C_{4}$ conformers and their corresponding energies were taken as zero value. If the entropic contributions were neglected the predicted conformational equilibrium for (**1**) could contain about 96% of the $^{1}C_{4}$ form and that for (**2**) would be composed of 90% $^{1}C_{4}$ and 10% $^{4}C_{1}$ and $^{o}S_{2}$. However, it is known[9] that the entropy term can be higher for skew-boat conformations and the free energy difference between the chair-like, $^{1}C_{4}$, and the skew-boat, $^{o}S_{2}$, conformations could be smaller than calculated.

The proton–proton torsion angles to be expected for the $^{1}C_{4}$, $^{o}S_{2}$, and $^{4}C_{1}$ forms of (**1**), and (**2**), deduced from the MM2 calculations, are shown in Table 13 and the expected values of the proton–proton vicinal coupling constants for these conformers, calculated according to the equation of Altona,[6] are given in Table 14. A conformational mixture containing approximately 90% of $^{1}C_{4}$ and 10% $^{4}C_{1}$ and $^{o}S_{2}$ forms could account for the experimental data for (**1**) at room temperature, the $^{1}C_{4}$ conformers being almost the exclusive form at – 100 °C (Table 10). In contrast, the data for compound (**2**) indicate that

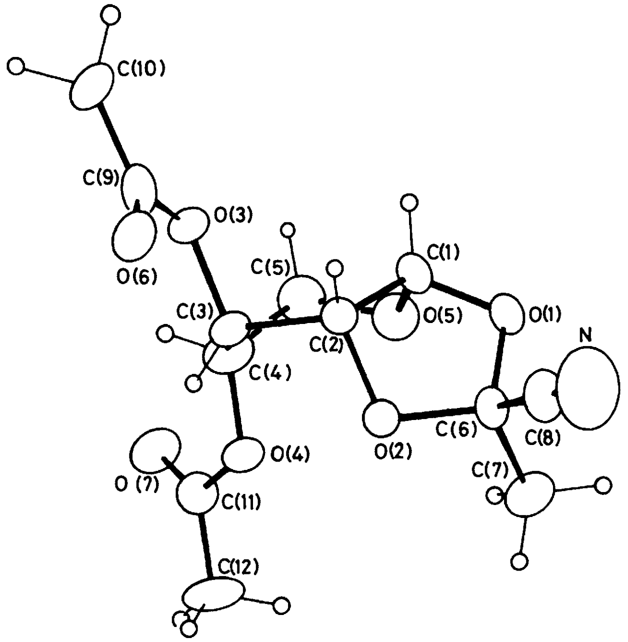


**Figure 2.** ORTEP[17] View of compound (**2**) showing the atomic numbering

**Table 2.** Bond lengths/Å for compounds (**1**) and (**2**). E.s.d.s in parentheses

| Bond | (**1**) | (**2**) |
|---|---|---|
| C(5)–O(5) | 1.434(5) | 1.424(5) |
| C(1)–O(1) | 1.410(4) | 1.400(4) |
| C(3)–O(3) | 1.440(5) | 1.443(4) |
| C(6)–O(1) | 1.409(6) | 1.429(4) |
| C(1)–C(2) | 1.507(6) | 1.516(4) |
| C(3)–C(4) | 1.520(5) | 1.522(4) |
| C(6)–C(8) | 1.505(6) | 1.493(5) |
| C(8)–N | 1.129(7) | 1.130(6) |
| C(11)–O(4) | 1.352(5) | 1.340(4) |
| C(11)–O(7) | 1.197(4) | 1.195(5) |
| C(11)–C(12) | 1.476(9) | 1.485(6) |
| C(1)–O(5) | 1.414(5) | 1.412(4) |
| C(2)–O(2) | 1.439(4) | 1.435(3) |
| C(4)–O(4) | 1.438(5) | 1.444(4) |
| C(6)–O(2) | 1.400(7) | 1.411(4) |
| C(2)–C(3) | 1.523(6) | 1.519(4) |
| C(4)–C(5) | 1.509(7) | 1.506(5) |
| C(6)–C(7) | 1.509(5) | 1.491(5) |
| C(9)–O(3) | 1.357(6) | 1.355(4) |
| C(9)–O(6) | 1.178(6) | 1.200(5) |
| C(9)–C(10) | 1.438(8) | 1.476(6) |

the conformational equilibrium consists, in this case, of a high proportion of skew-boat conformers (>90%) which become almost exclusive at low temperature. Additional evidence indicating the major $^{o}S_{2}$ conformation of the pyranoid ring of (**2**) was obtained from n.O.e. experiments. Irradiation of the signal assigned to the *endo*-methyl group in the $^{1}H$ n.m.r. spectrum of (**2**) induced a 7% increase of the integrated intensity of the signal assigned to 5-$H_{ax.}$ as expected for a major $^{o}S_{2}$ conformation.

With regard to the corresponding ethylidene derivatives (**3**) and (**4**), the proton–proton coupling constants and similar n.O.e. evidence as that described for compound (**2**) demonstrated that the major solution conformation of the pyranoid ring of compound (**4**) at room temperature must also be a skew-boat $^{O}S_2$ conformation. On the other hand, the large $J_{2,3}$ and $J_{3,4}$ values observed in the $^1$H n.m.r. spectrum of compound (**3**) indicated an important contribution of conformers in which the pyranoid ring shows a chair-like $^4C_1$ form (Table 12) and the solution conformation of this compound at room temperature may be composed of $^4C_1$, $^1C_4$, and $^{O}S_2$ forms in an approximately 2:2:1 ratio.

According to the above results it can be concluded that the conformation of the pyranoid ring of 1,2-*O*-alkylidene-α-D-xylopyranoses in solution strongly depends on the substituent at C(2) of the dioxolane ring. The small contribution of the $^4C_1$ form to the conformational equilibria of compounds (**1**), (**2**), and (**4**) could be explained as a result of the steric interaction between the *endo*-substituent at C(2) of the dioxolane ring and H(3). The anomeric effect does not seem to have an important influence on the conformation of the pyranoid ring as it would favour $^4C_1$ or $^{O}S_2$ conformations in contrast to our *X*-ray results, which demonstrate that the pyranoid rings of both compounds (**1**) and (**2**) present a $^1C_4$ conformation in the solid state, and our n.m.r. spectroscopic results which indicate a similar $^1C_4$ major solution conformation of the pyranoid ring of compound (**1**). Table 15 shows some selected torsion angles deduced from MM2 calculations for the conformers $^1C_4$ of (**1**) and $^{O}S_2$ of (**2**). It is also interesting to note that, although care should be taken when the energy values provided by molecular mechanics calculations are considered, these calculations give a satisfactory qualitative explanation of the distribution of conformers and of the geometry of these when compared with the results obtained from n.m.r. spectroscopic parameters.

The application of carbon–proton coupling constants to the conformational analysis of organic compounds, although highly desirable, has not yet been satisfactorily developed owing to the scarcity of reliable published data.[10] After the development of new n.m.r. techniques these parameters can be

**Table 3.** Bond angles/° for compounds (**1**) and (**2**). E.s.d.s in parentheses

| Angle | (**1**) | (**2**) |
|---|---|---|
| C(5)–O(5)–C(1) | 113.0(3) | 112.4(3) |
| O(5)–C(1)–C(2) | 114.0(3) | 112.5(3) |
| C(1)–C(2)–C(3) | 117.1(3) | 115.5(3) |
| C(3)–C(4)–C(5) | 111.2(3) | 111.1(3) |
| C(4)–C(3)–O(3) | 105.3(3) | 102.6(2) |
| C(5)–C(4)–O(4) | 110.6(3) | 111.1(3) |
| C(2)–C(1)–O(1) | 103.0(2) | 102.9(3) |
| C(2)–O(2)–C(6) | 108.3(3) | 106.4(2) |
| O(1)–C(6)–O(2) | 107.6(3) | 107.2(2) |
| O(1)–C(6)–C(7) | 110.3(4) | 112.5(3) |
| O(2)–C(6)–C(7) | 111.8(4) | 110.4(3) |
| C(6)–C(8)–N | 174.4(4) | 178.3(5) |
| C(4)–O(4)–C(11) | 117.5(3) | 116.3(3) |
| C(4)–C(11)–O(7) | 122.6(4) | 123.1(3) |
| O(4)–C(11)–C(12) | 114.4(4) | 111.4(3) |
| O(7)–C(11)–C(12) | 126.0(5) | 125.5(3) |
| O(5)–C(1)–O(1) | 106.0(2) | 106.1(3) |
| O(5)–C(5)–C(4) | 110.4(3) | 111.2(3) |
| C(2)–C(3)–C(4) | 113.6(4) | 113.7(2) |
| C(2)–C(3)–O(3) | 107.0(3) | 107.0(2) |
| C(3)–C(4)–O(4) | 105.2(3) | 107.3(3) |
| C(3)–C(2)–O(2) | 109.4(3) | 109.9(2) |
| C(1)–C(2)–O(2) | 103.3(3) | 101.3(2) |
| C(1)–O(1)–C(6) | 106.2(3) | 107.9(2) |
| O(1)–C(6)–C(8) | 109.9(3) | 105.7(3) |
| O(2)–C(6)–C(8) | 108.6(4) | 108.7(3) |
| C(8)–C(6)–C(7) | 108.6(3) | 112.0(3) |
| C(3)–O(3)–C(9) | 116.4(3) | 118.0(3) |
| O(3)–C(9)–O(6) | 122.4(4) | 122.4(3) |
| O(3)–C(9)–C(10) | 111.2(4) | 110.4(3) |
| O(6)–C(9)–C(10) | 126.4(5) | 127.2(3) |

**Table 5.** Final atomic co-ordinates for compound (**1**)

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 0.326 3(3) | 0.149 7(4) | 0.275 4(3) |
| O(2) | 0.320 6(3) | 0.339 2(4) | 0.344 4(3) |
| O(3) | 0.158 1(3) | 0.438 2(4) | −0.145 5(3) |
| O(4) | −0.062 1(3) | 0.390 8(4) | 0.161 5(3) |
| O(5) | 0.057 9(3) | 0.182 0(4) | 0.656(3) |
| O(6) | 0.339 2(5) | 0.581 8(5) | −0.017 9(5) |
| O(7) | −0.343 2(3) | 0.396 6(5) | −0.003 5(5) |
| N | 0.092 8(5) | 0.193 0(5) | 0.544 2(6) |
| C(1) | 0.229 8(4) | 0.204 7(0) | 0.100 9(5) |
| C(2) | 0.279 4(4) | 0.329 4(5) | 0.142 4(5) |
| C(3) | 0.146 0(4) | 0.419 2(5) | 0.036 0(5) |
| C(4) | −0.035 2(4) | 0.378 8(5) | −0.012 9(5) |
| C(5) | −0.058 1(4) | 0.255 1(4) | −0.078 9(5) |
| C(6) | 0.336 2(4) | 0.228 1(5) | 0.420 9(5) |
| C(7) | 0.501 3(6) | 0.212 6(7) | 0.591 9(6) |
| C(8) | 0.191 8(5) | 0.207 6(5) | 0.482 9(6) |
| C(9) | 0.265 5(4) | 0.522 8(4) | −0.150 9(6) |
| C(10) | 0.275 8(7) | 0.528 6(7) | −0.340 9(8) |
| C(11) | −0.224 4(5) | 0.396 4(5) | 0.147 1(6) |
| C(12) | −0.232 5(7) | 0.401 7(7) | 0.337 5(9) |

**Table 6.** Final atomic co-ordinates for compound (**2**)

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 0.630 1(1) | 0.270 4(2) | 0.167 6(4) |
| O(2) | 0.569 5(1) | 0.355 1(1) | −0.110 5(3) |
| O(3) | 0.423 8(1) | 0.449 2(1) | 0.282 9(4) |
| O(4) | 0.586 5(1) | 0.561 2(1) | 0.008 4(4) |
| O(5) | 0.632 1(1) | 0.413 9(2) | 0.319 9(4) |
| O(6) | 0.335 1(1) | 0.390 9(2) | 0.039 0(5) |
| O(7) | 0.591 6(2) | 0.703 7(2) | 0.158 7(6) |
| N | 0.575 7(3) | 0.129 0(3) | −0.249 3(10) |
| C(1) | 0.582 2(2) | 0.337 5(2) | 0.271 5(6) |
| C(2) | 0.521 7(2) | 0.359 8(2) | 0.089 8(5) |
| C(3) | 0.483 0(2) | 0.455 2(2) | 0.107 3(6) |
| C(4) | 0.538 3(2) | 0.530 6(2) | 0.195 9(6) |
| C(5) | 0.588 8(2) | 0.494 6(3) | 0.386 7(7) |
| C(6) | 0.626 7(2) | 0.285 2(2) | −0.071 2(5) |
| C(7) | 0.704 8(2) | 0.313 4(3) | −0.167 7(8) |
| C(8) | 0.597 5(2) | 0.195 8(2) | −0.169 7(8) |
| C(9) | 0.350 6(2) | 0.418 1(2) | 0.225 6(7) |
| C(10) | 0.296 6(3) | 0.423 7(4) | 0.421 5(9) |
| C(11) | 0.607 7(2) | 0.651 3(2) | 0.008 4(6) |
| C(12) | 0.655 2(3) | 0.675 0(3) | −0.195 1(9) |

**Table 4.** Geometry of the short intramolecular contacts/Å, ° from *X*-ray diffraction data

| | (**1**) | (**2**) | | (**1**) | (**2**) |
|---|---|---|---|---|---|
| O(2)–C(2) · · · C(4)–O(4) | −4.1(5) | 2.8(2) | C(9)–O(3)–C(3)–H(3) | 28(2) | 35(2) |
| O(2) · · · O(4) | 3.074(3) | 3.083(3) | O(7) · · · C(4) | 2.674(5) | 2.650(4) |
| O(6) · · · C(3) | 2.645(7) | 2.240(4) | O(7) · · · H(4) | 2.47(5) | 2.30(4) |
| O(6) · · · H(3) | 2.24(4) | 2.44(3) | O(7)–C(11)–O(4)–C(4) | −3.2(7) | 3.6(5) |
| O(6)–C(9)–O(3)–C(3) | 3.5(7) | 4.1(5) | C(11)–O(4)–C(4)–H(4) | 44(3) | 28(3) |
| C(3)–H(3) · · · O(6) | 104(3) | 96(2) | C(4)–H(7) · · · O(7) | 92(3) | 102(3) |

**Table 7.** Configurational angles[1]/°, mod 2π for the non-hydrogen first substituents at the chiral centres of the pyranoid ring, following the sequence: ··· C(1),C(2) ···

| | (1) | | (2) | |
|---|---|---|---|---|
| Angle | Value | Type | Value | Type |
| [C(1)–O(1)] | 112.6(6) | α | 118.8(5) | α |
| [C(2)–O(2)] | 120.3(6) | Xylose | 118.7(5) | Xylose |
| [C(3)–O(3)] | −115.7(6) | Xylose | −112.5(5) | Xylose |
| [C(4)–O(4)] | 119.7(7) | D | 121.7(6) | D |
| [C(6)–C(8)] | 118.1(7) | *endo* | −115.8(6) | *exo* |

**Table 8.** $^1H$ N.m.r. data (δ from $Me_4Si$; *J*/Hz) for compounds (**1**)—(**4**)

| Proton | (**1**) | (**2**) | (**3**) | (**4**) |
|---|---|---|---|---|
| 1 | 5.517 | 5.661 | 5.375 | 5.391 |
| 2 | 4.030 | 4.296 | 4.044 | 3.903 |
| 3 | 5.390 | 5.257 | 5.262 | 5.194 |
| 4 | 4.725 | 4.878 | 4.759 | 4.826 |
| $5_{eq.}$ | 4.060 | 3.591 | 3.870 | 3.727 |
| $5_{ax.}$ | 3.871 | 3.972 | 3.691 | 3.821 |
| $J_{1.2}$ | 3.1 | 4.6 | 4.1 | 4.9 |
| $J_{2.3}$ | 2.8 | 2.8 | 4.4 | 2.9 |
| $J_{2.4}$ | 1.0 | 1.0 | 0.0 | 1.0 |
| $J_{3.4}$ | 3.8 | 2.9 | 5.6 | 2.9 |
| $J_{3.5eq.}$ | 1.0 | 0.0 | 0.0 | 0.0 |
| $J_{4.5eq.}$ | 3.5 | 8.0 | 4.6 | 8.3 |
| $J_{4.5ax.}$ | 2.4 | 6.0 | 6.3 | 5.9 |
| $J_{5eq..5ax.}$ | −12.5 | −11.5 | −12.2 | −12.0 |

**Table 9.** Observed and calculated $^3J_{HH}$/Hz for compounds (**1**) and (**2**)

| | | (**1**) | (**2**) |
|---|---|---|---|
| $J_{1.2}$ | observed[a] | 3.1 | 4.5 |
| | calculated[b] | 3.0 | 2.9 |
| $J_{2.3}$ | observed | 2.8 | 2.8 |
| | calculated | 3.1 | 3.1 |
| $J_{3.4}$ | observed | 3.8 | 2.9 |
| | calculated | 2.7 | 2.4 |
| $J_{4.5eq.}$ | observed | 3.5 | 6.0 |
| | calculated | 2.1 | 2.3 |
| $J_{4.5ax.}$ | observed | 2.4 | 8.0 |
| | calculated | 1.3 | 1.7 |

[a] In $CDCl_3$ solution. [b] From *X*-ray data by Altona's equation.

**Table 10.** Temperature dependence/°C for $^3J_{HH}$/Hz of compounds (**1**) and (**2**) in acetone–methanol (4:1)

| | | Temperature/°C | | | | |
|---|---|---|---|---|---|---|
| *J*/Hz | | 20 | −25 | −50 | −75 | −100 |
| 1,2 | (**1**) | 3.4 | 3.2 | 2.9 | 2.8 | 2.6 |
| | (**2**) | 4.4 | 4.4 | 4.6 | 4.6 | 4.7 |
| 2,3 | (**1**) | 3.4 | 3.2 | 3.0 | 2.6 | 2.6 |
| | (**2**) | 2.8 | 2.6 | 2.6 | 2.6 | 2.6 |
| 3,4 | (**1**) | 3.6 | 3.4 | 3.3 | 3.2 | 3.2 |
| | (**2**) | 3.0 | 2.6 | 2.5 | 1.8 | <1 |
| 4,5*eq.* | (**1**) | | | | 2.0 | 1.5 |
| | (**2**) | 7.7 | 7.9 | 8.1 | 8.3 | 8.5 |
| 4,5*ax.* | (**1**) | | | | 2.0 | 1.5 |
| | (**2**) | 5.7 | 5.0 | 6.2 | 6.5 | 6.8 |

**Table 11.** $^{13}C$ N.m.r. spectral parameters δ (p.p.m.) (from $Me_4Si$) and *J*/Hz for compounds (**1**) and (**2**) in acetone solution

| Carbon | (**1**) | (**2**) |
|---|---|---|
| 1 | 97.3 | 98.1 |
| 2 | 75.9 | 75.9 |
| 3 | 66.9 | 69.2 |
| 4 | 65.9 | 68.3 |
| 5 | 61.9 | 60.6 |
| 6 | 99.9 | 100.5 |
| *J*/Hz | | |
| C(1), H(1) | 178.2 | 181.2 |
| C(2), H(2) | 158.5 | 155.7 |
| C(3), H(3) | 152.3 | 154.6 |
| C(4), H(4) | 155.3 | 153.1 |
| C(5), H(5*eq.*) | 152.6 | 150.4 |
| C(5), H(5*ax.*) | 145.7 | 147.5 |
| C(1), H(2) | 0.9 | 2.4 |
| C(2), H(1) | 7.3 | 5.7 |
| C(2), H(3) | −4.9 | −5.6 |
| C(3), H(2) | −4.0 | −4.5 |
| C(3), H(4) | −4.5 | −5.0 |
| C(4), H(3) | −5.0 | −4.2 |
| C(4), H(5*eq.*) | −5.1 | −1.0 |
| C(4), H(5*ax.*) | −1.8 | −4.7 |
| C(5), H(4) | −1.3 | −2.9 |
| C(1), H(3) | 4.0 | 4.7 |
| C(1), H(5*eq.*) | 7.6 | 6.2 |
| C(1), H(5*ax.*) | 4.0 | 5.0 |
| C(2), H(4) | 3.4 | 3.2 |
| C(3), H(1) | 0.9 | 1.0 |
| C(3), H(5*eq.*) | 4.7 | 4.8 |
| C(3), H(5*ax.*) | 1.8 | 2.7 |
| C(4), H(2) | 3.1 | 4.2 |
| C(5), H(1) | 1.9 | 5.3 |
| C(5), H(3) | 3.5 | 2.0 |
| C(6), H(1) | 7.4 | 3.9 |
| C(6), H(2) | 1.4 | 0.0 |

**Table 12.** Relative 'steric[8] energies'/kcal $mol^{-1}$ for the local minima of compounds (**1**) and (**2**) corresponding to the $^1C_4$, $^oS_2$, and $^4C_1$ pyranoid ring conformations from MM2 calculations[7]

| | $^1C_4$ | $^oS_2$ | $^4C_1$ |
|---|---|---|---|
| (**1**) | 0 | 2.96 | 1.84 |
| (**2**) | 0 | 1.39 | 1.85 |

**Table 13.** Proton–proton torsion angles for the $^1C_4$, $^oS_2$, and $^4C_1$ conformations from MM2 calculations[7]

| | (**1**) | | | (**2**) | | |
|---|---|---|---|---|---|---|
| $\Phi_{HH}$/° | $^1C_4$ | $^oS_2$ | $^4C_1$ | $^1C_4$ | $^oS_2$ | $^4C_1$ |
| 1,2 | −42 | −24 | 38 | −44 | −21 | 40 |
| 2,3 | −73 | −61 | −162 | −71 | −62 | −161 |
| 3,4 | 70 | 93 | 175 | 71 | 87 | 172 |
| 4,5*eq.* | −59 | −30 | −61 | −61 | −25 | −61 |
| 4,5*ax.* | 60 | −148 | 179 | 58 | −144 | 179 |

determined without much difficulty. We have determined long-range proton–carbon spin coupling constants from heteronuclear 2D *J*-resolved experiments using the selective proton π pulse described by Bax and Freeman[11] which permits the observation of long-range $^1H$–$^{13}C$ couplings between the carbon atoms and the irradiated proton in the *F*1 dimension. Table 16 presents the proton–carbon torsion angles for the major solution conformations of (**1**) and (**2**) which can be related to heteronuclear coupling constants. The observed $^3J_{C,H}$ values show a Karplus-like relationship and allowed the unequivocal assignment of the signals for 5-$H_{ax}$ and 5-$H_{eq}$ since $J_{C\text{-}1,5\text{-}H_{eq}}$ and $J_{C\text{-}3,5\text{-}H_{eq}}$ were larger than $J_{C\text{-}1,5\text{-}H_{ax}}$ and $J_{C\text{-}3,5\text{-}H_{ax}}$ respectively. Similarly $J_{C\text{-}5,1\text{-}H}$ was larger for compound (**2**), the major conformation of the pyranoid ring of

**Table 14.** Proton–proton coupling constants for the $^1C_4$, $^\circ S_2$, and $^4C_1$ conformations according to Altona and MM2 calculations[7]

| | (1) | | | (2) | | |
|---|---|---|---|---|---|---|
| $^3J_{HH}$/Hz | $^1C_4$ | $^\circ S_2$ | $^4C_1$ | $^1C_4$ | $^\circ S_2$ | $^4C_1$ |
| 1,2 | 2.8 | 4.6 | 5.0 | 2.6 | 4.9 | 4.9 |
| 2,3 | 2.2 | 3.9 | 8.3 | 2.7 | 3.6 | 7.9 |
| 3,4 | 2.6 | 0.7 | 9.3 | 2.4 | 0.9 | 9.1 |
| 4,5*eq.* | 2.7 | 8.7 | 4.9 | 2.7 | 9.1 | 4.9 |
| 4,5*ax.* | 0.9 | 8.3 | 10.6 | 1.1 | 7.7 | 10.6 |

**Table 15.** Selected torsion angles for the $^1C_4$ conformer of (**1**) and $^\circ S_2$ conformer of (**2**) from MM2 calculations[7]

| Angle | (**1**) | (**2**) |
|---|---|---|
| C(1)–C(2)–C(3)–C(4) | 41.2 | 52.6 |
| C(2)–C(3)–C(4)–C(5) | −49.3 | −30.2 |
| C(3)–C(4)–C(5)–O(5) | 62.9 | −27.3 |
| C(4)–C(5)–O(5)–C(1) | −65.5 | 68.2 |
| C(5)–O(5)–C(1)–C(2) | 55.2 | −44.5 |
| O(5)–C(1)–C(2)–C(3) | −43.0 | −16.4 |
| O(1)–C(1)–C(2)–O(2) | −38.7 | −19.1 |
| C(1)–C(2)–O(2)–C(6) | 26.2 | 34.5 |
| C(2)–O(2)–C(6)–O(1) | −4.6 | −38.2 |
| O(2)–C(6)–O(1)–C(1) | −21.5 | 25.9 |
| C(6)–O(1)–C(1)–C(2) | 35.4 | −3.7 |
| C(1)–C(2)–C(3)–O(3) | −78.9 | −67.3 |
| C(2)–C(3)–C(4)–O(4) | 71.7 | 92.2 |
| C(5)–O(5)–C(1)–O(1) | 167.6 | 75.9 |
| O(5)–C(1)–C(2)–O(2) | 80.5 | 104.1 |

**Table 16.** X–H Torsion angles from MM2 calculations[7] for (**1**) $^1C_4$, and (**2**) $^\circ S_2$

| $\Phi_{X,H}$/° | (**1**) | (**2**) |
|---|---|---|
| C(1), H(3) | 162 | 173 |
| C(1), H(5*eq.*) | 175 | −171 |
| C(1), H(5*ax.*) | 59 | 56 |
| C(2), H(4) | −168 | −151 |
| C(3), H(1) | 82 | 103 |
| C(3), H(5*eq.*) | 180 | −145 |
| C(3), H(5*ax.*) | −60 | 96 |
| C(4), H(2) | 165 | 177 |
| C(5), H(1) | −72 | −166 |
| C(5), H(3) | −171 | −151 |
| C(6), H(1) | 155 | 115 |
| C(6), H(2) | −89 | −83 |
| O(1), H(2) | 75 | 96 |
| O(5), H(2) | −167 | −141 |
| O(2), H(1) | −155 | −136 |
| O(2), H(3) | 45 | 57 |
| O(3), H(2) | 46 | 57 |
| O(3), H(4) | −48 | −30 |
| O(4), H(3) | −51 | −29 |
| O(4), H(5*eq.*) | 58 | 94 |
| O(4), H(5*ax.*) | 178 | −25 |
| O(5), H(4) | −178 | 93 |

which is a skew-boat ($\Phi_{C(5),H(1)} = -166°$), then for compound (**1**), whose pyranoid ring is predominantly a chair ($\Phi_{C(5),H(1)} = -72°$). These vicinal couplings are larger across oxygen than across carbon atoms for the same value of torsion angle. The $^3J_{C,H}$ values provide information to investigate the conformation of the dioxolane rings in solution. It has been reported[12] that the acetal carbon of dioxolane-type benzylidene acetals *cis*-fused to pyranoid rings shows heteronuclear coupling only with the axially oriented bridgehead proton and that this coupling can be correlated with the conformation of the dioxolane ring. The observed value of these couplings for compounds (**1**) and (**2**) demonstrated (Table 4) that the dioxolane rings of both compounds have different conformations. The large value of $J_{C\text{-}6,1\text{-}H}$ observed for (**1**) might indicate a torsion angle of *ca.* 180° between these atoms, and the small value $J_{C\text{-}6,2\text{-}H}$ could be assigned to a torsion angle of *ca.* 90°. Both values are compatible with a $E_1$ conformation of the dioxolane ring with th pyranoid ring in the $^1C_4$ conformation. For compound (**2**), the intermediate $J_{C\text{-}6,1\text{-}H}$ value and the zero $J_{C\text{-}6,2\text{-}H}$ value might be interpreted in terms of a $E_{O2}$ conformation of the dioxolane ring with the pyranoid ring in the $^\circ S_2$ conformation.

Finally, geminal $^2J_{C,H}$ values were also determined (Table 4). These coupling constants are also related to the orientation of the electronegative substituent on the carbon atom and can take positive and negative values.[13,14] *gauche*-Oxygen–proton torsion angles give values between −4 and −5 Hz while larger angles decrease the absolute values of these couplings.

## Experimental

Optical rotations were determined with a Perkin-Elmer 141 polarimeter. T.l.c. was performed on silica gel $GF_{254}$ (Merck) with detection by charring with sulphuric acid.

Compounds (**1**) and (**2**) were prepared by methods described in the literature.[15] Compounds (**3**) and (**4**) were prepared as reported by Betaneli *et al.*[16] for the D-mannopyranose analogue: *endo–exo* mixture (2:1) (73%) (Found: C, 50.6; H, 6.2. $C_{11}H_{16}O_7$ requires C, 50.8; H, 6.2%); $[\alpha]_D$ +4° (*c* 0.8, in $CHCl_3$).

*Crystal Data.*—(**1**): $C_{12}H_{15}NO_7$, $M$ = 285.25, transparent prisms (0.33 × 0.23 × 0.17 mm), monoclinic, space group, $P2_1$, $a$ = 8.560 8(2), $b$ = 116.087(4), $c$ = 7.600 6(2) Å, $\beta$ = 113.111(2)°, $D_c$ = 1.364 g cm$^{-3}$, $Z$ = 2. Cell parameters obtained from a least squares fit using 79 reflections, with $\theta$ up to 45° and Cu-$K_\alpha$ radiation.

(**2**): Same formula as compound (**1**) and shape (0.27 × 0.30 × 0.40 mm), orthorhombic, space group $P2_12_12_1$, $a$ = 16.866 4(10), $b$ = 14.347 2(6), $c$ = 5.913 5(1) Å, $D_c$ = 1.384 g cm$^{-3}$, $Z$ = 4. Cell parameters as for compound (**1**) with 90 reflections.

*Data Collection.*—Both compounds were analysed in a PW 1100 four circles diffractometer with Cu-$K_\alpha$ radiation, graphite-monochromated, $\omega/2\theta$ scans, 1.5° scan width and 1 min per reflection. Good stability for both samples checked every 90 min. With a $3\sigma(I)$ criterion (**1**) gave 1 109 observed reflections and (**2**) 12 780, up to $\theta$ = 65°.

*Solution and Refinement.*—The structures were solved by direct methods[18] and refined by one block matrix least squares procedures[19] for 240 and 241 parameters respectively. All hydrogen atoms were localised in a different synthesis and included isotropically. An empirical weighting scheme, so as to give no trends in $\langle w\Delta^2F\rangle$ *vs.* $\langle|F_{obs.}|\rangle$ or $\sin\langle\theta/\lambda\rangle$, was introduced. The final shift/error was 0.09 and 0.11 with maximum peaks in the final $\Delta F$ of 0.11 and 0.16 e Å$^{-3}$. The maximum thermal factors were $U22$ [C(7)] = 0.119(4) and $U11$ [C(12)] = 0.106(3) Å$^2$ for (**1**) and (**2**) respectively. Final $R$ and $R_w$ factors were 0.034, 0.039, and 0.042, 0.045, respectively.

All calculations were performed on a VAX 11/750 computer. The atomic scattering factors were taken from reference 20.

*N.m.r. Data.*—$^1$H n.m.r. spectra (internal $Me_4Si$) were recorded in $CDCl_3$ solution on a Varian XL-300 spectrometer. Analyses were performed by using a PANIC program. The experimental and calculated spectra from the resulting best values matched satisfactorily. $^{13}C$ N.m.r. spectra (internal $Me_4Si$) were recorded on the same spectrometer, in acetone solution. Long-range carbon–proton coupling constants were determined by selective heteronuclear 2D-*J*-resolved spectra[11] by using the proton flip technique with decoupler pulse intensity $\frac{\gamma B_2}{2\pi} = 40$ Hz, and length of 8.5 ms for the 90° pulse. The fully-coupled spectrum was finally computer-assisted simulated by using a PANIC program with *X*-approximation.

*Molecular Mechanics Calculations.*—It was necessary to provide two parameters for torsion angles not included in the program data, namely, $C_{sp}$–$C_{sp^3}$–O–$C_{sp^3}$ and $C_{sp}$–$C_{sp^3}$–O–LP ($V_1 = 0$, $V_2 = 0$, $V_3 = 0.2$) and one bending parameter for the angle $C_{sp}$–$C_{sp^3}$–O [$K(B) = 0.98$, THETA (O) = 108.5]. The default value for the bulk dielectric constant (1.5 D) corresponding to the gas phase was substituted by a value (10 D), stated as a good effective ε for $Cl_3CH$.

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