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# A $^{13}$C-N.M.R. STUDY OF 1,6:2,3- AND 1,6:3,4-DIANHYDRO-β-D-HEXOPYRANOSES AND THEIR *O*-ACETYL AND DEOXY DERIVATIVES

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## ABSTRACT

$^{13}$C-N.m.r. spectra of all possible 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses and their *O*-acetyl and deoxy derivatives are presented. Relations between chemical shifts of certain carbon atoms and the structure of the dianhydrides are outlined, and their application in structural analysis is discussed. Inversion of configuration of the oxirane ring from the *endo* to the *exo* position is associated with typical upfield-shifts for oxirane-ring carbon atoms C-2 or C-4, respectively. Possible interrelationships between $^{13}$C-chemical shifts and steric and polar interactions in the dianhydro derivatives are discussed.

## INTRODUCTION

Recently, some data demonstrating the effectiveness of $^{13}$C-n.m.r. spectroscopy for structural analysis of oxirane derivatives of pyranoses have been presented[1]. We now report on the $^{13}$C-n.m.r. spectra of all of the 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses and their *O*-acetyl and deoxy derivatives **1–12**. These compounds constitute a complete series having a very rigid, tricyclic skeleton, with the pyranoid ring in the $^5H_O$(D) or $^1H_O$(D) conformation. Consequently, they are convenient models in studying physical and chemical properties of oxirane derivatives, and are useful intermediates in syntheses[2]. In addition to the free dianhydrides, their *O*-acetyl derivatives also proved to be suitable compounds for spectroscopic examination, since they can be prepared easily under conditions that preclude isomerisation of the starting dianhydrides. Moreover, due to the β-effect of the acetoxyl group[3], the position of the oxirane ring can be detected by a comparison of the spectra of free and acetylated compounds.

The method of selective, double, heteronuclear resonance ($^{13}$C{$^1$H}) has been used for assignment of the $^{13}$C signals, combined with double-resonance $^1$H–$^1$H measurements in some instances.

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## RESULTS AND DISCUSSION

For all the dianhydrides **1**–**12**, the C-1 carbon atoms display the highest chemical shifts (97–102 p.p.m.); the signals for C-5 are shifted upfield by 26–30 p.p.m. (see Tables I and II). The oxirane-ring carbon atoms resonate at ~46–58 p.p.m. A pair of signals in this region of the spectrum is a reliable criterion for the presence of the oxirane ring[1,4,5]. In comparison, the carbon atoms in 1,6-anhydro-β-D-hexopyranoses[6–8] corresponding to oxirane-ring carbon atoms in the title dianhydrides are shifted downfield by ~8–24 p.p.m.

TABLE I

$^{13}$C-N.M.R. CHEMICAL SHIFTS[a] OF 1,6:2,3- AND 1,6:3,4-DIANHYDRO-β-D-HEXOPYRANOSES AND THEIR DEOXY DERIVATIVES IN SOLUTION IN $CDCl_3$

| *Compound* | | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* |
|---|---|---|---|---|---|---|---|
| 2,3-*talo*[b] | **1a** | 98.2 | 58.4 | 51.1 | 67.15 | 72.1 | 63.9 |
| 2,3-*manno* | **2a** | 97.7 | 54.3 | 49.4 | 67.0 | 74.2 | 65.7 |
| 2,3-*allo* | **3a** | 97.2 | 49.2 | 50.2 | 66.5 | 78.0 | 65.0 |
| 2,3-*gulo* | **4a** | 96.9 | 48.8 | 53.1 | 63.1 | 73.3 | 63.4 |
| 3,4-*talo* | **5a** | 98.1 | 66.8 | 50.4 | 57.3 | 71.8 | 64.05 |
| 3,4-*galacto* | **6a** | 100.8 | 65.8 | 50.0 | 53.0 | 72.2 | 65.0 |
| 3,4-*allo*[b] | **7a** | 102.6 | 65.9 | 49.4 | 50.6 | 69.5 | 65.9 |
| 3,4-*altro* | **8a** | 100.8 | 68.1 | 52.45[c] | 51.5[c] | 71.0 | 66.7 |
| 2,3-*lyxo* | **9** | 98.1 | 53.8 | 46.3 | 30.2 | 67.3 | 68.4 |
| 2,3-*ribo* | **10** | 97.2 | 48.6 | 47.6 | 30.1 | 71.15 | 68.8 |
| 3,4-*lyxo* | **11** | 97.25 | 31.6 | 46.2 | 52.8 | 72.4 | 64.2 |
| 3,4-*ribo* | **12** | 99.45 | 32.0 | 46.3 | 50.5 | 69.5 | 66.5 |

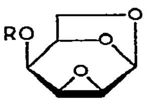
[a] Chemical shifts in p.p.m. downfield from internal tetramethylsilane. [b] In $CD_3OD$. [c] Assignments may be interchangeable.

TABLE II

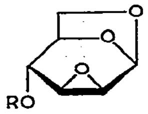
$^{13}$C-N.M.R. CHEMICAL SHIFTS[a] OF ACETATES OF 1,6:2,3- AND 1,6:3,4-DIANHYDRO-β-D-HEXOPYRANOSES IN SOLUTION IN $CDCl_3$

| *Compound* | | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* | *$CH_3$(Ac)* | *CO(Ac)* |
|---|---|---|---|---|---|---|---|---|---|
| 2,3-*talo* | **1b** | 97.3 | 57.6 | 47.8 | 68.4 | 68.4 | 63.8 | 20.9 | 170.2 |
| 2,3-*manno* | **2b** | 97.9 | 54.3 | 47.5 | 68.7 | 71.5 | 65.8 | 20.9 | 170.2 |
| 2,3-*allo* | **3b** | 97.2 | 47.9 | 47.5 | 68.9 | 75.1 | 65.6 | 20.7 | 170.5 |
| 2,3-*gulo* | **4b** | 97.1 | 48.1 | 50.6 | 65.2 | 71.0 | 63.8 | 20.7 | 169.4 |
| 3,4-*talo* | **5b** | 95.9 | 69.2 | 47.7 | 55.9 | 71.8 | 64.4 | 20.6 | 170.3 |
| 3,4-*galacto* | **6b** | 98.3 | 66.9 | 48.0 | 52.7 | 71.95 | 64.7 | 20.8 | 170.7 |
| 3,4-*allo* | **7b** | 100.1 | 67.9 | 46.7 | 49.2 | 69.5 | 65.5 | 20.5 | 170.3 |
| 3,4-*altro* | **8b** | 97.1 | 67.3 | 49.2 | 49.8 | 69.9 | 67.3 | 20.6 | 169.9 |

[a] Chemical shifts in p.p.m. downfield from internal tetramethylsilane.



1a R = H
b R = Ac



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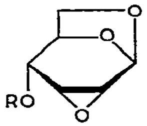
b R = Ac



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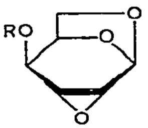
b R = Ac



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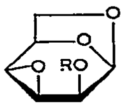
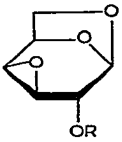
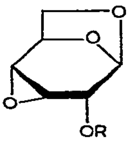
b R = Ac



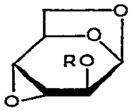
5a R = H
b R = Ac



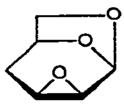
6a R = H
b R = Ac



7a R = H
c R = Ac



8a R = H
b R = Ac



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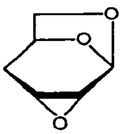

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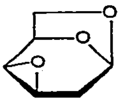

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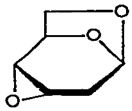

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It is remarkable that the chemical shifts for the oxirane-ring C-3 (in comparison with those for C-2 and C-4) do not depend markedly on the position and configuration of the oxirane ring and the neighbouring substituent, and lie in a rather narrow range, namely, 49.4–53.1, 46.7–50.6, and 46.2–47.6 p.p.m. for free, acetylated, and deoxy compounds, respectively. On the other hand, the chemical shifts for the oxirane-ring C-2 or C-4 vary within the limits 48–58 p.p.m.

Markedly high values of chemical shifts (~53–58 p.p.m.) were observed for C-2 in **1** and **2**, and C-4 in **5** and **6**, *i.e.* for compounds having an *endo*-oriented* oxirane ring; the highest chemical shifts occurred for dianhydrides **1** and **5**, where the oxirane ring and the vicinal hydroxyl group are *cis* to the 1,6-anhydride bond (see Tables I and II).

In the dianhydrides **1a**, **2a**, **5a**, and **6a**, inversion of the configuration of the oxirane ring from the *endo* to the *exo* position results in upfield chemical-shifts of the signals for C-2 or C-4 by 2.4–9.6 p.p.m. (see Table III). Similar trends were observed for the acetylated dianhydrides.

For the *endo*-dianhydrides **1** and **5**, inversion of the configuration at the carbon atom bearing the hydroxyl group causes a small upfield-shift for this carbon, not exceeding 1 p.p.m., whereas the signals for C-2 or C-4, which form part of the oxirane ring, are shifted upfield by 4.1–4.3 p.p.m. A quite different situation exists for the *exo*-

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**Endo* and *exo* designate the *cis* or *trans* position, respectively, with regard to the 1,6-anhydride bond.

TABLE III

DIFFERENCES IN CHEMICAL SHIFTS FOR C-2, C-3, AND C-4 IN DIANHYDRIDES, RELATED TO THE INVERSION OF CONFIGURATION OF THE OXIRANE RING

| *Configurational change* | *Chemical shift (p.p.m.) for*[a] | | |
|---|---|---|---|
| | *C-2* | *C-3* | *C-4* |
| **1a**→ **4a** | +9.6 | −2.0 | +4.05 |
| **2a**→ **3a** | +5.1 | −0.8 | +0.5 |
| **5a**→ **8a** | −1.3 | −2.05 | +5.8 |
| **6a**→ **7a** | −0.1 | +0.6 | +2.4 |
| **9** →**10** | +5.2 | −1.3 | +0.1 |
| **11** →**12** | −0.4 | −0.1 | +2.3 |

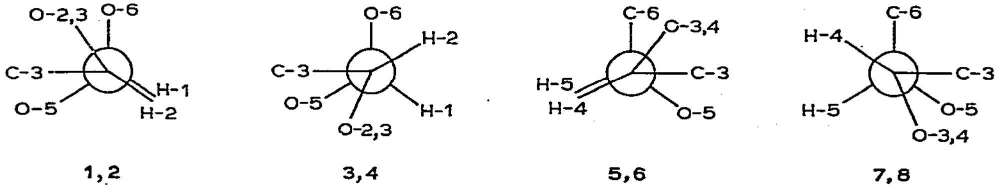
[a]Signs + and — designate the upfield or downfield shift, respectively.

TABLE IV

DIFFERENCES IN CHEMICAL SHIFTS FOR C-2, C-3, AND C-4 IN DIANHYDRIDES, RELATED TO THE INVERSION OF CONFIGURATION OF THE HYDROXYL GROUP ADJACENT TO THE OXIRANE RING

| *Configuration change* | *Chemical shift (p.p.m.) for*[a] | | |
|---|---|---|---|
| | *C-2* | *C-3* | *C-4* |
| **1a**→**2a** | +4.1 | +0.7 | +0.15 |
| **5a**→**6a** | +1.0 | +0.4 | +4.3 |
| **4a**→**3a** | −0.4 | +2.9 | −3.4 |
| **8a**→**7a** | +2.2 | +3.05 | +0.9 |

[a]Signs + and — designate the upfield or downfield shift, respectively.



Scheme 1

dianhydrides **4** and **8**, where the corresponding chemical shifts are larger for the α-carbon (—3.4 and +2.2 p.p.m.) and far less for the oxirane-ring carbons (—0.4 and +0.9) (see Table IV).

Differences in chemical shifts for C-2 and C-4, summarised in Table III, may originate from steric and polar interactions between the 1,6-anhydride bond, the oxirane ring, and adjacent hydroxyl or acetyl groups (see Scheme 1). Increased crowding of the oxirane-ring oxygen in an *endo* position, and O-6 or C-6 of the 1,6-

TABLE V

DIFFERENCES IN CHEMICAL SHIFTS FOR C-2 OR C-4 OF THE OXIRANE RING, RELATED TO STERIC AND POLAR INTERACTIONS OF OXYGEN-CONTAINING GROUPS IN DIANHYDRIDES AND THEIR DEOXY DERIVATIVES

| *Type of interaction* | *Downfield shift (p.p.m.)* |
|---|---|
| 2,3-*endo* Oxirane-ring/1,6-anhydride bond | ~5.2[a] |
| 3,4-*endo* Oxirane-ring/1,6-anhydride bond | ~2.3[b] |
| *endo* OH-Group *cis* to oxirane ring | ~4.2 |
| *exo* OH-Group *cis* to oxirane ring | ~1[c] |
| *endo* or *exo* OH-Group *trans* to oxirane ring | ~0[d] |
| *exo* Oxirane-ring/1,6-anhydride bond | ~0[d] |

[a] Chemical shift for C-2. [b] Chemical shift for C-4. [c] Downfield or upfield shift; see Table IV. [d] This value has been set arbitrarily.

anhydride bond (see compounds **1**, **2**, **5**, and **6** in Scheme 1), may lead to a distortion of the molecule, particularly of the oxirane ring, and result in a high downfield-shift, the highest value being observed for C-2 in **1**, where O-2(3), O-4, and O-6 adopt an eclipsed-like position. Similar observations have been reported for some *cis* and *trans* methyl-substituted derivatives of steroid oxiranes[4,5]. Inversion of the configuration of the *endo* oxirane-ring and/or *endo* hydroxyl-group in **1**, **2**, **5**, and **6**, to give **3**, **4**, **7**, and **8**, must result in a lessening of steric crowding (see Scheme 1) and is manifested in upfield shifts (see Tables III and IV). This conclusion accords with the observation on 2,3-*exo* and 2,3-*endo* epoxides of the norbornane series[9], where the oxirane-ring carbon atoms in the *endo* compound are shifted by ~11 p.p.m. downfield with regard to the *exo* compound.

Inspection of the data in Tables III and IV permits a tentative inter-relation of configurational changes with the observed differences in chemical shifts for the oxirane-ring carbon atoms C-2 or C-4 (see Table V). Thus, the values obtained for the inversion of the configuration of the 2,3-*endo* oxirane-ring (5.1 p.p.m.) and 3,4-*endo* oxirane-ring (2.4 p.p.m.) fit very well with the values (5.2 and 2.3 p.p.m., respectively) obtained for deoxy derivatives **9–12** (see Table III).

Presumably, the magnitude of these differences in chemical shifts, which obviously reflect steric and polar interactions of the oxirane ring (see Scheme 1), might be correlated with the energy content* of the dianhydrides and, consequently, used for an approximate assessment of their thermodynamic stability. This possibility can be illustrated by the equilibrated mixtures of **2a** $\rightleftharpoons$ **8a** and **6a** $\rightleftharpoons$ **4a**, where the preponderance of **8a** and **4a**, respectively, can be predicted (*cf.* Ref. 10) by using the data in Table V. The summation of interactions (expressed in chemical shifts) is ~5.2 for **2a**, ~2.3 for **6a**, and ~0 p.p.m. for **4a** and **8a**. According to the literature[11,12],

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*However, this seems not to be true for the average of the chemical shift for all six carbon atoms, *cf.* Ref. 7.

the equilibrated mixture **2a** ⇌ **8a** contains more than 95% of **8a**, and **6a** ⇌ **4a** contains 80% of **4a**.

From the data in Tables I and II, it follows that $^{13}$C-n.m.r. spectroscopy may be useful for identification of all the dianhydro derivatives mentioned above. For example, the 2,3-epoxides **1a**–**4a** can be easily distinguished from their 3,4-isomers **5a**–**8a** by comparison of their spectra with those of the corresponding acetates. Upfield shifts of the signals of C-5 (2.3–3.7 p.p.m.) for the first, and of C-1 (2.3–3.7 p.p.m.) for the second, group permit both types to be distinguished.

A difference not exceeding 2 p.p.m. between the chemical shifts for the signals of the oxirane-ring carbon atoms is characteristic for *exo*-epoxides **3a**, **7a**, and **8a**. For **3a** and **7a**, the signals of C-5 and C-1, respectively, appear at lowest field. Compounds **4a** and **7a** can be easily identified, the former by the presence of a pair of signals ($\Delta$ 0.3 p.p.m.) for C-4 and C-6, the latter through coincidence of the signals for C-2 and C-6. Epoxides **2a**,**8a** and **4a**,**6a**, which tend to isomerise in alkaline solution, are also easily identifiable in their equilibrium mixtures.

## EXPERIMENTAL

The $^{13}$C-n.m.r. spectra for solutions in $CDCl_3$ and $CD_3OD$ (internal $Me_4Si$) were recorded with a Bruker WP-60 instrument in the Fourier-transform mode at 15.08 MHz, using 4/8K data points, a pulse interval of 1.1 sec, and a pulse flipping angle of 30°. Selective decoupling, $^{13}C_i\{^1H_i\}$ experiments were made after the determination of proton chemical shifts by $^1$H-n.m.r. spectroscopy. $^1$H-N.m.r. spectra for the dianhydrides **1**–**12** were measured with a Varian HA-100 spectrometer at 100 MHz and have been published elsewhere[13]. The synthesis of the dianhydro derivatives and their acetates has been described elsewhere[11,13–16].

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