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ASSESSMENT OF THE VALUES OF THE C–H-STRETCHING FORCE CONSTANTS IN SUGAR MOLECULES

STEFANIA PIZZINI, GIUSEPPE BAJO, SERGIO ABBATE*,
Istituto di Chimica delle Macromolecole del C.N.R., via Bassini 15a, 20133 Milano (Italy)

GIUSEPPINA CONTI,
Istituto "G. Donegani", via Fauser 4, Novara (Italy)

AND RAJAI H. ATALLA
The Institute of Paper Chemistry, P.O. Box 1039, Appleton, WI 54912 (U.S.A.)

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ABSTRACT

I.r. and Raman spectra of *epi*-inositol, *muco*-inositol, *myo*-inositol, methyl α-D-glucopyranoside, methyl α-D-glucopyranoside-*2,3,4,6,6'-*d_5, methyl α-D-mannopyranoside, and methyl α-D-mannopyranoside-*2,3,4,6,6'-*d_5 have been recorded in the C–H stretching region. The frequencies of the observed bands are interpreted in terms of a linear equation relating the stretching force constant to the dihedral angle formed by the C–H bond with the lone pairs of electrons on the closest oxygen atom. The usefulness of the equation in the conformational analysis of carbohydrates is considered.

INTRODUCTION

The dependence of the C–H-stretching diagonal force constant K_{CH} on the conformation relative to the lone pairs of electrons of the oxygen atom nearest to the C–H bond has been proposed[1] and applied[2] to α- and β-D-glucose. The complexity of i.r. and Raman spectra in the C–H-stretching region of these compounds in the solid state was attributed to the non-equivalence of the various C–H *local* oscillators. On the same basis, the differences between the spectra of α- and β-D-glucose in the region 2800–3000 cm^{-1} were interpreted in a straightforward manner.

The above explanation is useful in interpreting the C–H stretching region of other carbohydrates in the solid state, and i.r. and Raman spectra could be useful for obtaining information about the conformations of the OH groups when the structure of the molecule cannot be derived by other techniques (X-ray or neutron diffraction, n.m.r. spectroscopy).

We have proposed an empirical equation[3] which allows K_{CH} to be determined from the known conformation of an adjacent oxygen atom. The equation is

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*Author for correspondence.

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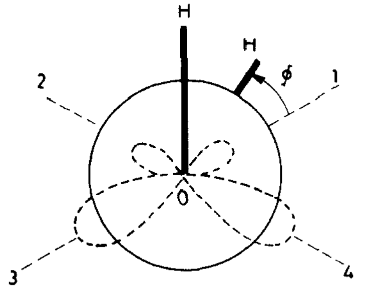


Fig. 1. Newman projection of the HCOH fragment and definition of the dihedral angle ϕ appearing in equation *1*.

$$K(\phi) = \frac{K_G - K_T}{60^\circ}\phi + K_T, \qquad (1)$$

where $K_G = K(60^\circ)$ if the C–H bond is *gauche* to the lone pairs of the oxygen atom and $K_T = K(0^\circ)$ if the C–H bond is *trans* to the major lobe of either lone pair of the oxygen atom and $0 < \phi < 60^\circ$. Fig. 1 shows a Newman projection of an HCOH fragment. Hitherto, equation *1* was regarded as applicable only when the C–H bond was between reference lines 1 and 2. However, it has been shown[2] that when a C–H bond is *cis* to the major lobe of a lone pair, it has the same force constant as it does when it is *trans*. Thus, equation *1* should be valid also when a C–H bond is between reference lines 3 and 4. The conformations of the C–H bond which are not covered by equation *1* are between reference lines 1 and 4 and 2 and 3, namely, when the conformation of the C–H bond is in between *trans* and *cis* with respect to the lone pair. The values for K_G and K_T depend on the type of oxygen atom (ether, alcohol, *etc.*) nearest to the C–H bond and they are chosen to best reproduce the i.r. and Raman frequencies of prototype molecules.

We have applied equation *1* to two groups of molecules, namely, *epi*-, *muco*-, and *myo*-inositol, and methyl α-D-glucopyranoside, methyl α-D-mannopyranoside, and their 2,3,4,6,6′-d_5 derivatives.

Since inositols contain only HCOH groups, they are ideal for characterizing C–H bonds adjacent to O–H groups and the conclusions reached can be transferred easily to C–H bonds at positions 1–4 of methyl α-D-hexopyranosides.

RESULTS

Inositols. — *myo*-Inositol was a commercial product, *epi*-inositol was obtained from Professor L. Anderson (University of Wisconsin at Madison), and *muco*-inositol was obtained from its di-*O*-isopropylidene derivative[4].

(*a*) *Spectra.* Raman spectra were measured with a SPEX 1401 Raman

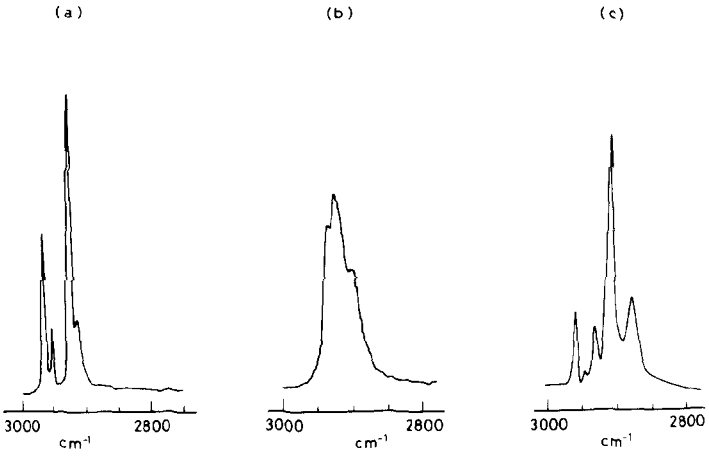


Fig. 2. Raman spectra in the C–H stretching region of (a) *epi*-inositol (at 70 K), (b) *muco*-inositol (at 300 K), and (c) *myo*-inositol (at 70 K). Ordinate axes are not reported.

spectrometer (Appleton). The radiation source was a Coherent Radiation Model 52 A Ar^+ laser (514.5 nm) and the slit widths were set for a minimum resolution of 5 cm^{-1}. Fig. 2 shows Raman spectra in the C–H stretching region for *muco*-inositol at room temperature and for *epi*- and *myo*-inositol at liquid N_2 temperature. Pressed pellets of the compounds were placed in a 180° back-scattering platform for the room-temperature experiments and in a 90° configuration in a Harney–Miller temperature control cell for the 70-K experiment[4].

I.r. spectra were recorded on a Perkin–Elmer Model 621 grating i.r. spectro-

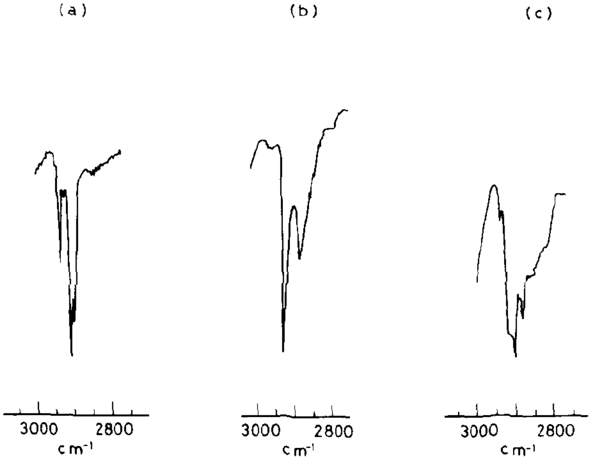
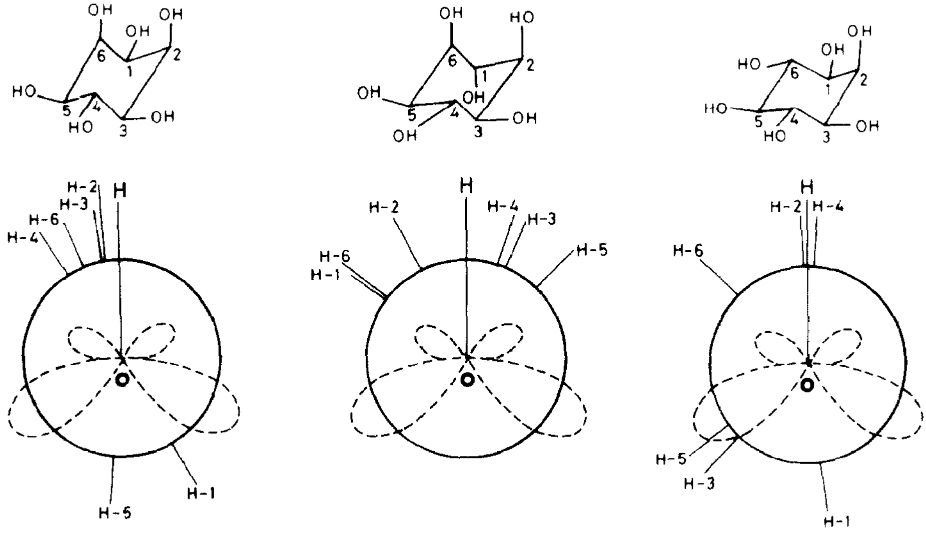


Fig. 3. I.r. transmittance spectra in the C–H stretching region of (a) *epi*-inositol (at 70 K), (b) *muco*-inositol (at 300 K), and (c) *myo*-inositol (at 70 K). Ordinate axes are not reported.

meter. For the spectra in the C–H stretching region, the samples were prepared as Fluorolube mulls with capillary thickness between CaF_2 plates. The average resolution was comparable with that of the Raman experiment. These spectra are given in Fig. 3. When available, the low-temperature spectra are better resolved, although they are comparable with those obtained at room temperature.

(*b*) *Normal co-ordinate calculations.* Matrices **B** and $\mathbf{G}^5$ for *epi-*, *muco-*, and *myo*-inositol have been calculated using X-ray crystal structures[6–8]. Because of the large experimental uncertainties in the co-ordinates of hydrogen atoms, the O–H and C–H bond lengths were set at 0.97 and 1.1 Å, respectively, retaining only the experimental orientation. The force field reported by Williams[4], which was obtained with the Fletcher–Powell algorithm, was used for all the internal co-ordinates except for the C–H stretchings. The C–H-stretching force constants were assigned using equation *1* where the values for ϕ were derived from X-ray structures. Fig. 4 shows Newman projections for the six HOCH groups in the three molecules. Using a trial-and-error procedure, it was found that the values for K_T and K_G of 4.540 and 4.770 mdyne/Å, respectively, best reproduce the observed C–H stretching frequencies. These values are lower than those found for ethanol (K_T = 4.594, K_G = 4.784 mdyne/Å), for which no explanation can be offered. Interaction force constants f'_G, f'_T, f''_G, and f''_T for the various C–H bonds up to the second nearest neighbour were added[2]. The latter force constants are effective in delocalizing C–H stretching motions (see below).



epi-Inositol *muco*-Inositol *myo*-Inositol

Fig. 4. Newman projections of HCOH groups in crystalline *epi*-inositol, *muco*-inositol, and *myo*-inositol, as viewed from O to C (---- lone pairs).

TABLE I

OBSERVED AND CALCULATED FREQUENCIES IN THE C–H STRETCHING REGION FOR INOSITOLS

ν_{obs} (cm^{-1}) (at 70 K)		ν_{calc}	*Assignment*[a]
I.r.	*Raman*		
epi-*Inositol*			
2960	2964	2963	C-5-H (C-3-H,C-2-H)
		2953	C-2-H (C-5-H,C-3-H)
2942	2949	2947	C-3-H (C-1-H,C-2-H,C-5-H)
2930	2922	2926	C-6-H (C-1-H)
2918	2912	2921	C-4-H
2905		2908	C-1-H (C-6-H,C-5-H,C-3-H)
muco-*Inositol*			
2970			
		2942	C-3-H (C-2-H)
2938	2936	2939	C-4-H (C-3-H)
	2927	2926	C-2-H (C-3-H,C-1-H)
		2908	C-5-H (C-6-H,C-3-H)
2893	2900	2900	C-1-H (C-6-H,C-5-H,C-2-H)
		2888	C-6-H (C-1-H,C-5-H)
myo-*Inositol*			
2959	2962	2964	C-1-H (C-2-H,C-3-H)
		2961	C-4-H (C-2-H)
	2946	2956	C-2-H (C-1-H,C-3-H,C-4-H)
2928	2937		
2917	2919	2927	C-3-H (C-1-H,C-2-H)
	2907	2908	C-6-H (C-4-H,C-5-H)
2895	2900	2895	C-5-H (C-3-H,C-1-H,C-6-H)

[a] The bonds reported in parentheses refer to minor contributions.

Table I contains the Raman and i.r. data together with the calculated frequencies and assignments.

Methyl α-D-hexopyranosides. — Methyl α-D-glucopyranoside, its *2,3,4,6,6'-d_5* derivative, and methyl α-D-mannopyranoside were commercial products. Methyl α-D-mannopyranoside-*2,3,4,6,6'-d_5* was prepared at the Istituto Biochimico "G. Ronzoni" (Milano), using a Raney Nickel catalyst.

(*a*) *Spectra.* I.r. spectra were recorded for KBr pellets, using a FTIR Bruker spectrometer (128 scans were taken with a resolution of 2 cm^{-1}). The glycosides were analyzed in the region 2800–3100 cm^{-1} and the deuterated compounds also in the C–D stretching region (2300–2100 cm^{-1}). Raman spectra were taken on finely powdered samples in capillary tubes, using a Jarrel–Ash spectrometer (Milano). The exciting line was the 488.0-nm line of a Ar^+ Spectra Physics laser. The scattered radiation was viewed at 90° to the incident beam. The Raman spectra of the manno-

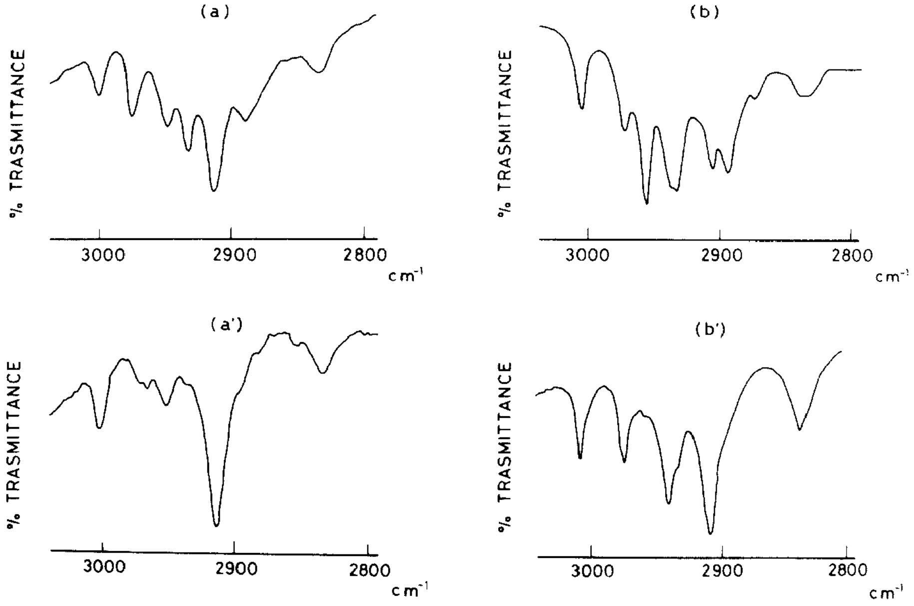


Fig. 5. I.r. transmittance spectra in the C–H stretching region of (a) methyl α-D-glucopyranoside, (a') its 2,3,4,6,6'-d_5 derivative, (b) methyl α-D-mannopyranoside, and (b') its 2,3,4,6,6'-d_5 derivative. Ordinate axes are not reported.

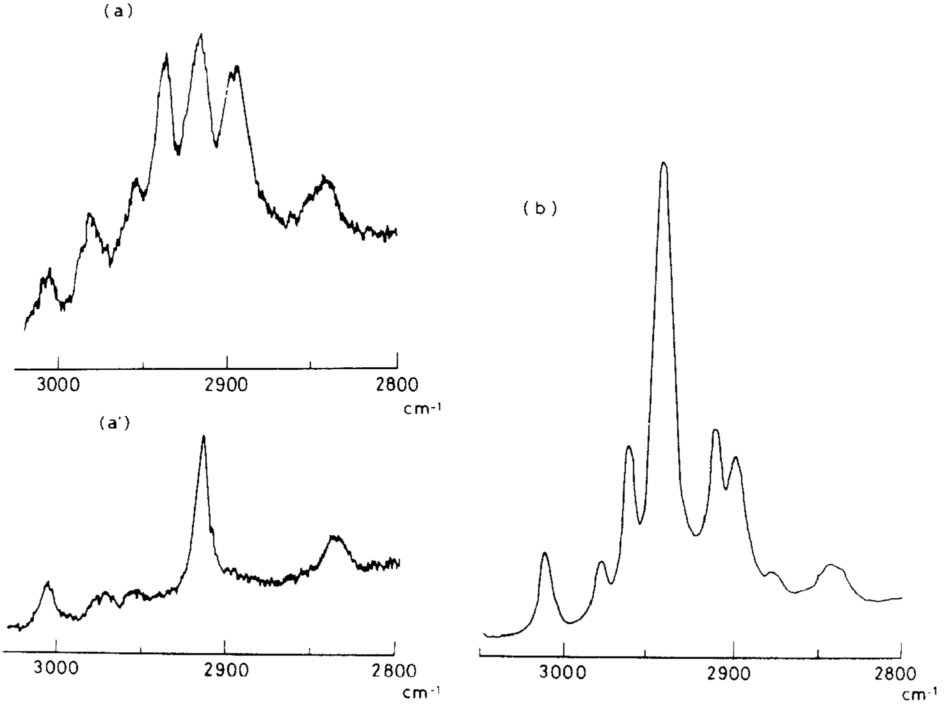


Fig. 6. Raman spectra in the C–H stretching region of (a) methyl α-D-glucopyranoside, (a') its 2,3,4,6,6'-d_5 derivative, and (b) methyl α-D-mannopyranoside. Ordinate axes are not reported.

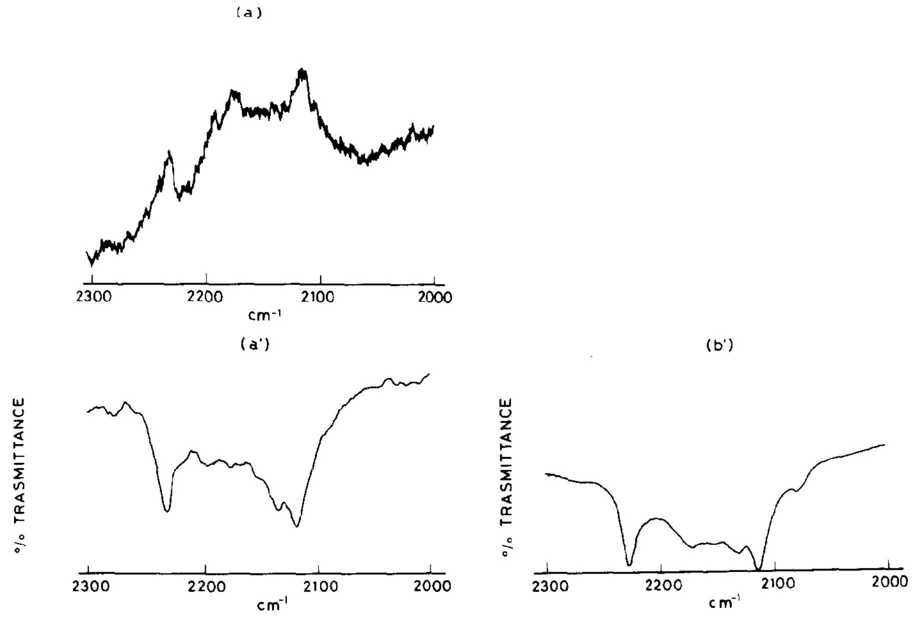


Fig. 7. Raman (a) and i.r. (a′) spectra of methyl α-D-glucopyranoside-2,3,4,6,6′-d_5 and i.r. spectrum (b′) of methyl α-D-mannopyranoside-2,3,4,6,6′-d_5 in the C–D stretching region. Ordinate axes are not reported.

pyranoside-d_5 could not be recorded due to strong fluorescence. The i.r. and Raman spectra in the C–H stretching region are shown in Figs. 5 and 6, respectively. The Raman spectra of the glucopyranosides were recorded under the following conditions: counts per second (c.p.s.), 5×10^3; resolution, 5 cm^{-1}; scanning speed, 20 cm^{-1}/min; time constant, 2 s; laser power, 30 mW.

The conditions for the mannopyranosides were as follows: c.p.s., 10^4; resolution, 5 cm^{-1}; time constant, 10 s; scanning speed, 10 cm^{-1}/min; laser power, 40 mW.

Fig. 7 shows the i.r. and Raman spectra in the C–D stretching region of the d_5 compounds. The i.r. spectra were taken with the same conditions as for the C–H stretching region. The Raman spectrum was obtained with the following settings: c.p.s., 2×10^3; resolution, 3 cm^{-1}; scanning speed, 10 cm^{-1}/min; laser power, 120 mW.

(*b*) *Normal co-ordinate calculations.* The spectra of perhydrogenated compounds in the C–H stretching region were complex because of the great number of C–H oscillators. The construction of a C–H-stretching force field is complicated by the presence of two types of C–H bond (close to hydroxyl and ether oxygen, respectively). Moreover, interactions of C–H stretching co-ordinates in $-CH_2OH$ and $-OCH_3$ groups add to the effect on the principal C–H-stretching force constant from a nearby oxygen atom.

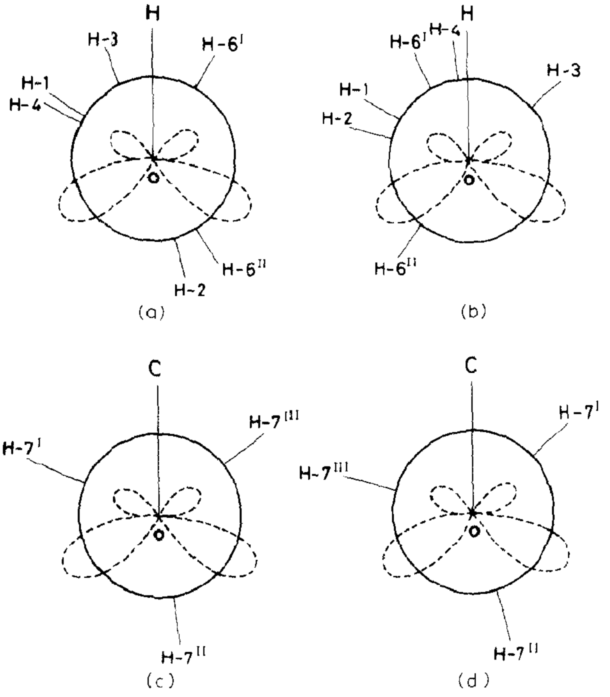


Fig. 8. Newman projections of HCOH groups of methyl α-D-glucopyranoside and methyl α-D-mannopyranoside as viewed from O to C (a and b) and of the C-1-O-1-CH_3 group in the same compounds as viewed from O-1 to the methyl carbon (c and d).

Matrices **B** and **G** for the hexopyranosides were calculated using neutron diffraction structures determined by Jeffrey *et al.*[9] and with no alterations. The force field reported by Vasko *et al.*[3] was used for all internal co-ordinates except for the C–H stretchings. The C–H-stretching force constants were assigned using equation *1*, where the values for ϕ were obtained from crystal structures (Fig. 8). For C–H bonds at positions 2, 3, 4, 6, and 6′, the values of K_T and K_G derived from the study of inositols were used. For the C-5-H bonds and for C–H bonds in the –OCH_3 group, values for K_T and K_G of 4.540 and 4.805 mdyne/Å, respectively, from dioxane[9] were used. The value for the C-1-H stretching force constant was an average between 4.805 mdyne/Å and the value obtained applying equation *1* to the ether-type oxygen, in order to account for the influence of the –OCH_3 group. The values used for methyl α-D-gluco- and -manno-pyranoside were 4.630 and 4.680 mdyne/Å, respectively.

Using a trial-and-error procedure and by comparing the spectra of the normal and partially deuterated compounds, the –CH_2OH and –OCH_3 groups could be characterized fully: the final values of the interaction force constants of adjacent C–H stretchings were 0.040 and −0.0041 mdyne/Å, respectively, for –OCH_3 and

TABLE II

OBSERVED AND CALCULATED FREQUENCIES IN THE C–H (C–D) STRETCHING REGION FOR METHYL α-D-GLUCOPYRANOSIDE

ν_{obs} (cm^{-1})		*ν_{calc} (cm^{-1})*	*Assignment*[a]
I.r.	*Raman*		
*Methyl α-*D*-glucopyranoside*			
3001	3004	3002	$\nu_{as}(-OCH_3)$
2975	2980	2965	$\nu_{as}(CH_2OH)$
		2965	$\nu_{as}(CH_2OH)$
2948	2950	2946	$\nu_{as}(-OCH_3)$
2933	2936	2932	C-3-H (C-5-H)
2913	2917	2917	C-1-H [C-2-H, $\nu_{as}(-OCH_3)$]
		2895	C-4-H & $\nu_{sym}(CH_2OH)$
2888	2893	2883	C-5-H [$\nu_{sym}(CH_2OH)$]
		2880	C-4-H [$\nu_{sym}(CH_2OH)$]
2834	2840	2816	$\nu_{sym}(-OCH_3)$
*Methyl α-*D*-glucopyranoside*-2,3,4,6,6′-d_5			
3001	3005	3002	$\nu_{as}(-OCH_3)$
(2970)	(2975)		
2950	(2950)	2946	$\nu_{as}(-OCH_3)$
2913	2916	2918	C-1-H
2895 sh		2887	C-5-H
2880 sh			
2832	2835	2816	$\nu_{sym}(-OCH_3)$
2231	2232	2220	$\nu_{as}(CD_2OH)$
2195	2190	2202	C-2-D
2175	2175	2176	C-3-D
2132		2142	C-4-D
2115	2118	2113	$\nu_{sym}(CD_2OH)$

[a] In parentheses are reported minor contributions.

–CH_2OH. In Tables II and III, the Raman frequencies are compared with the calculated frequencies, and the assignment of the observed bands is also reported.

DISCUSSION

Most of the i.r. and Raman bands in *epi*-, *muco*-, and *myo*-inositol are found above 2900 cm^{-1} (see Table I), due to the fact that the majority of C–H bonds are *gauche* to the oxygen lone-pairs which makes the force constant high (see Fig. 4). The results of the normal co-ordinate calculations are consistent with these experimental results. No other correlation was found. The stretching frequencies of corresponding C–H bonds in the various inositols were dissimilar (see Table I and the top of Fig. 4). The assignments in Table I are approximate since the full normal

TABLE III

OBSERVED AND CALCULATED FREQUENCIES IN THE C–H (C–D) STRETCHING REGION FOR METHYL α-D-MANNOPYRANOSIDE

ν_{obs} (cm^{-1})		ν_{calc} (cm^{-1})	*Assignment*[a]
I.r.	*Raman*		
Methyl α-D-mannopyranoside			
3006	3013	3004	ν_{as}(–OCH_3)
2975	2974	2970	ν_{as}(–OCH_3)
2959	2962	2959	ν_{as}(CH_2OH) (C-4-H)
2940	2943	2957	C-4-H [(ν_{as}(CH_2OH)]
2936		2936	C-1-H (C-2-H)
2911	2913	2908	C-2-H (C-1-H,C-3-H,C-5-H)
		2899	C-5-H,C-3-H,C-2-H [ν_{sym}(CH_2OH)]
2896	2901	2885	C-3-H, ν_{sym}(CH_2OH) (C-2-H,C-5-H)
2874	2878	2873	C-5-H, ν_{sym}(CH_2OH) (C-3-H)
2837	2840	2833	ν_{sym}(–OCH_3)
Methyl α-D-mannopyranoside-2,3,4,6,6′-d_5			
3003		3004	ν_{as}(–OCH_3)
2974		2970	ν_{as}(CH_2OH)
2940			
2931 sh		2935	C-1-H
2910		2886	C-5-H
2840		2833	ν_{sym}(–OCH_3)
2227		2216	ν_{as}(CD_2OH)
2171		2198	C-4-D (C-3-D)
2156		2155	C-2-D (C-3-D)
2132		2142	C-3-D (C-2-D,C-4-D)
2115		2108	ν_{sym}(CD_2OH)

[a] In parentheses are reported minor contributions.

co-ordinate calculations indicate delocalized motions, involving up to three centers[3].

The above spectral features are found also for *scyllo*- and *neo*-inositol[4] (for which normal co-ordinate calculations were not performed since no experimental crystal structures were available). Thus, the assessed importance of the angle HOCH in determining the C–H stretching frequencies leads to the assertion that, in crystalline *scyllo*- and *neo*-inositol also, most C–H bonds should be *gauche* to the nearby oxygen lone-pairs.

The assignments in Tables II and III for the methyl hexopyranosides show that the highest frequencies (>2955 cm^{-1}) correspond to asymmetric normal modes of the –OCH_3 and CH_2OH groups, whereas those lower than 2875 cm^{-1} correspond to symmetric modes.

The central frequencies correspond to stretchings of C–H bonds attached to the pyranose ring. In particular, the frequency "gap" between ~2940 and ~2910 cm^{-1} is reproduced nicely in both pyranosides. The sequence ν(C-2-H) > ν(C-3-H) > ν(C-4-H) found for methyl α-D-glucopyranoside is not the same as for α-D-glucose, mainly due to the different conformational property of C-4 (see Fig. 4 of ref. 2b). The frequencies for C-2-H and C-3-H are similar, the only difference being that the high value found for C-2-H seems to be consistent with the Raman spectrum of α-D-glucose-*2*-d_1. No such comparison is possible for methyl α-D-mannopyranoside.

The frequencies of C-1-H in methyl α-D-gluco- and -manno-pyranoside are different; no explanation is offered, although the predicted and experimental values are similar. Finally, C-5-H seems to have an unreasonably high stretching frequency in methyl α-D-mannopyranoside (~2910 cm^{-1}) which is at odds with the fairly general finding that C-5-H is influenced solely by O-5 such as to lower its frequency to ~2880 cm^{-1}, whenever the pyranose ring is in a $^4C_1$ conformation. These inconsistencies may be resolved when the Raman spectrum of methyl α-D-mannopyranoside-*2,3,4,6,6'*-d_5 is available.

Thus, the above C–H-stretching force field for monosaccharides relates dihedral angles for HCOH (HCOC) to the C–H stretching frequencies. The values for K_T and K_G of 4.540 and 4.770 mdyne/Å, respectively, characterize fairly well C–H bonds adjacent to OH groups, through equation *1*. Similar conclusions were reached in our previous work on α- and β-D-glucose[2], though not on a quantitative basis. The conclusion that the values for K_T and K_G are lower than the corresponding values for ethanol is based on ~50 frequency data. The absolute values for interaction C–H-stretching force constants in the groups $-OCH_3$ and $-CH_2OH$ are also lower than those found in ethers[10] and used for D-glucose.

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