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Carbohydrate Research 271 (1995) C1–C5

CARBOHYDRATE RESEARCH

Preliminary communication

Ab Initio nuclear shielding calculations of a model α-(1 → 4)-glucan

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Received 10 February 1995; accepted 2 March 1995

Keywords: Amylose; α-(1 → 4)-Glucan

The ability to determine solid-state conformations of glycans is currently limited to materials in crystalline forms with experimental information from diffraction techniques. For less ordered materials, it would be anticipated that NMR spectroscopy could provide information on conformational states. Of particular interest are glycosidic conformations as these are the primary determinant of overall glycan shape. Due to the range of crystalline forms available for cyclodextrins and amylose, α-(1 → 4)-D-glucans have emerged as the most useful system for probing relationships between chemical shifts and glycosidic conformation. Solid state (CPMAS) NMR spectra of a variety of crystalline α-(1 → 4)-glucans exhibit conformationally dependent chemical shifts, particularly of the C-1 and C-4′ resonances. It has been suggested that this phenomenon is dependent upon the conformation at the glycosidic linkage and various correlations between chemical shift and structural features have been suggested [1–4]. Recently, these observations have been rationalised in terms of the anomeric effect [5].

In order to assess the potential for predicting (rather than correlating) ^{13}C chemical shifts, ab initio quantum mechanical nuclear shielding calculations (GIAO-CHF method [6,7]) have been performed on a model-α-(1 → 4)-glucan glycosidic linkage for the region of accessible glycosidic conformation [8]. The calculated absolute shieldings for the C-1 and C-4′ nuclei show a conformational dependence of up to 10 ppm which is in agreement with that found experimentally. Previous empirical correlations are shown to be predicted, and chemical shift maps for glycosidic conformations are constructed.

Due to the computationally intensive nature of ab initio calculations a model α linkage was employed (Fig. 1) the carbon atoms involved in the glycosidic linkage are

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SSDI 0008-6215(95)00116-6

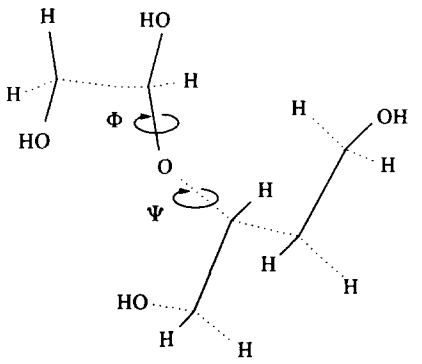

Fig. 1. Schematic representation of the model-α-(1 → 4)-glucan system.

termed pseudo C-1 and C-4′. The model was designed to simulate the electronic environment directly about the glycosidic linkage. For each calculation the conformation about the ϕ (H-1–C-1–O-1–C-4′) and ψ (H-4–C-4′–O-1–C-1) torsion angles was set and the shielding calculation performed without further optimisation of the structure so that only the dependence of the glycosidic conformation on nuclear shielding could be observed. This point has been discussed by de Dios and Oldfield [9]. Due to steric considerations at various torsion angle settings, slight optimisation of the groups involved was necessary but there was no change to the ϕ, ψ glycosidic conformation.

Two split-valence gaussian basis sets were used for the calculations. The 3-21G and 6-31G** levels [10]. The Biosym package Turbomole/TurboNMR was used as implemented on a Silicon Graphics Iris Indigo workstation to perform the 6-31G** level calculations while the program TX90 [7] was used as implemented on the Convex C3840 supercomputer at the University of London Computer Centre to perform the 3-21G level calculations. Calculations were performed varying the ψ torsion angle over the range $-60°$ to $+70°$ while keeping the ϕ torsion angle constant at 0°. A comparison of the results obtained from the 6-31G** and 3-21G basis sets for the C-1 (Fig. 2) and C-4′ (Fig. 3) nuclei show that even though the two sets of results are quantitatively different (as is expected when comparing these two basis sets) the observed trends are almost identical. In Figs. 2 and 3 we report C-13 nuclear shielding data rather than the chemical shifts usually observed by experiment. The two are related by an increase in one corresponding to a decrease in the other. The difference between C-1 and C-4′ values (approx 20 ppm) agrees well with experimental data. The local conformational origin of the observed effects was confirmed by the virtual invariance of shifts for atoms corresponding to C-2, C-3′, C-5′ and C-6′.

The C-1 and C-4′ nuclear shielding values were calculated for the conformational region ϕ, $-60°$ to $+60°$ and ψ, $-60°$ to $+60°$ at intervals of 30°. Contour maps were generated by the difference in shielding between the lowest calculated value ($\phi = \psi = 0°$) for both C-1 and C-4′ and that at each glycosidic conformation can be seen in Fig. 4 (for C-1) and Fig. 5 (for C-4′) at the 3-21G level. Even though the 3-21G level of basis set is not the best choice for nuclear shielding calculations, a comparison of the results obtained with those from the larger basis set (Figs. 2 and 3) shows almost identical

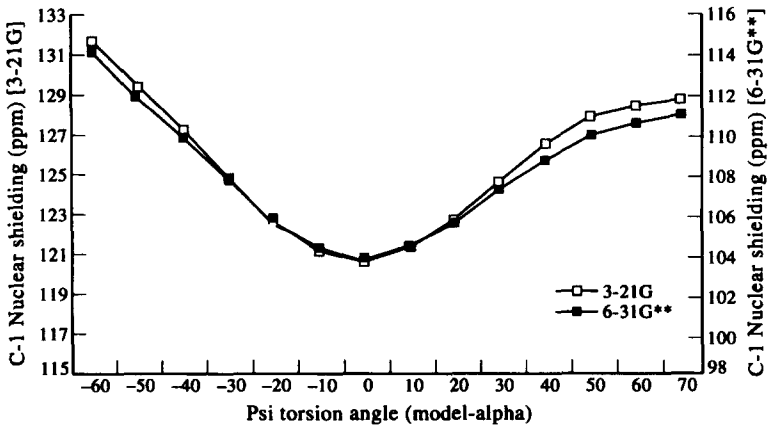

Fig. 2. Comparison of C-1 shieldings calculated using the 3-21G and 6-31G * * basis sets.

trends thus allowing an investigation of this important phenomenon with limited computational resources. The resulting shielding surfaces are consistent with previous empirical correlations and predict assignable experimental shifts. For C-1, observed shifts for V-amylose ($\phi - 14°$, $\psi - 7°$), A-amylose ($\phi - 25°$, $\psi - 32°$) and the $5 \rightarrow 6$ linkage in α-cyclodextrin hexahydrate ($\phi - 30°$, $\psi + 50°$) are [3] 103.5–104.0, 99–101 and 98.1 ppm respectively. From Fig. 4, calculated relative shifts are -1.5, -5.5 and -7.5 ppm. For C-4′, corresponding observed chemical shifts are [3] 82.2–83.2, 76.0 and 77.7 ppm, respectively, with calculated (Fig. 5) relative shifts of -1.7, -7.2 and -5.1 ppm. The reasonable correspondence (typically within 1 ppm) between observed and calculated relative shifts, supports the notion that glycosidic conformation is the primary determinant of the chemical shifts for glycosidic carbons in α-(1 → 4)-glucans. Previous empirical correlations [3] of C-1 shifts with (a) the modulus of ψ and (b) the

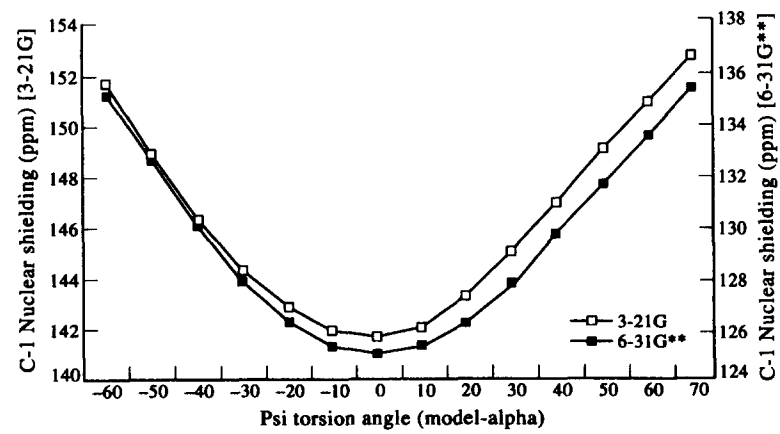

Fig. 3. Comparison of C-4′ shieldings calculated using the 3-21G and 6-31G * * basis sets.

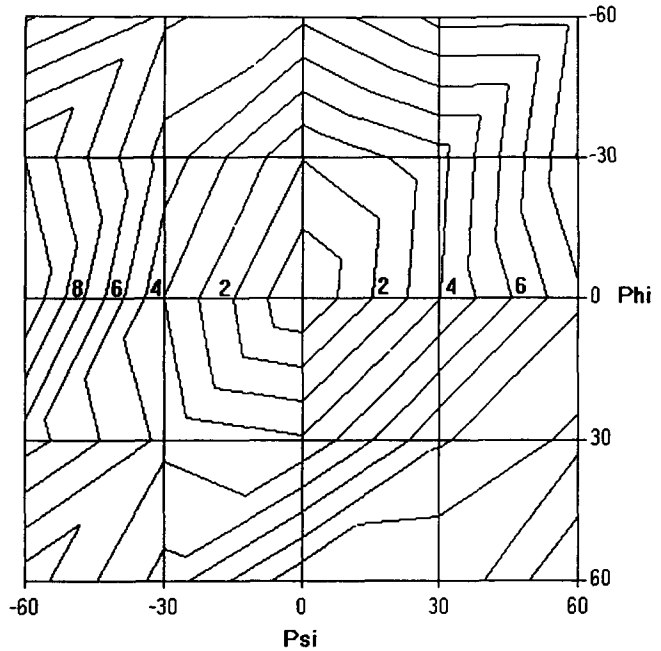

Fig. 4. Shielding surface for C-1 calculated at the 3-21G level with 1 ppm contour levels. The labels indicate the change in shielding (ppm) from the lowest calculated C-1 value ($\phi = \psi = 0°$).

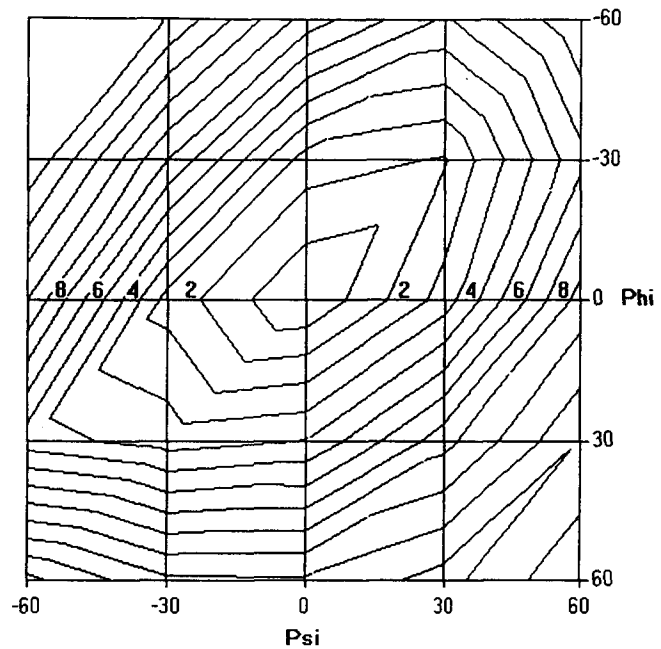

Fig. 5. Shielding surface for C-4′ calculated at the 3-21G level with 1 ppm contour levels. The labels indicate the change in shielding (ppm) from the lowest calculated C-4′ value ($\phi = \psi = 0°$).

sum of the moduli of ϕ and ψ, are now explicable in terms of (a) a near independence of ϕ over the experimental region (ϕ between +15 and +30) for different values of ψ and (b) a near diagonal symmetry in Fig. 4.

The reproduction of observed conformational shift effects by ab initio calculation demonstrates that such calculations are likely to prove useful in elucidating glycosidic conformations from non-crystalline materials. The generation of useful ϕ, ψ chemical shift maps with the relatively small 3-21G basis set indicates that only modest computational facilities may be needed in order to calculate realistic relative nuclear shieldings.

Acknowledgements

One of us, D.M.D. is grateful to Unilever Research for sponsorship. We are grateful to Professor J. Hinton (University of Arkansas) for a copy of TX90 and to ULCC for an allocation of Convex computer time.

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