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Citation: AIP Conference Proceedings **1267**, 104 (2010); doi: 10.1063/1.3482288
View online: http://dx.doi.org/10.1063/1.3482288
View Table of Contents: http://scitation.aip.org/content/aip/proceeding/aipcp/1267?ver=pdfcov
Published by the AIP Publishing

Raman Optical Activity of Biomacromolecules: Structural Analysis of Sugar Moieties in Glycoproteins

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During the last decade, the field of Raman optical activity (ROA) has expanded rapidly [1], mainly due to new developments in the theoretical calculations of the effect [2-5] and the commercialization of instrumentation [6]. ROA combines the conformational sensitivity of a chiral response with the structural information available in conventional vibrational spectroscopy and is ideally suited for detailed structural analysis of biomolecules in solution [7,8]. With the development of analytical derivatives of the ROA property tensors [3,4], predicting ROA spectra of model compounds of a biologically relevant size has proved feasible [7,9]. These analytical derivatives have now been included in the computational programme suites Gaussian 09 and Dalton [10,11], which commonly enables the prediction of ROA spectra. Hence, a dual approach in the analysis of solution structures of biomolecules, using both experimental and predicted ROA spectra ought to be adopted as the current standard in the field.

Carbohydrates and glycoproteins have previously been shown to be excellent samples for ROA experiments [12]. In the present study, we combine ROA measurements of complex carbohydrates and glycoproteins in solution with theoretical studies of relevant glycan moieties of glycoproteins, in order to examine the solution conformation of this important group of biomacromolecules.

The experimental Raman and ROA spectra of the mannose-rich glycoprotein yeast invertase are presented in Figure 1 together with the corresponding spectra of the mannose trisaccharide α-D-Man*p*-(1→2)-α-D-Man*p*-(1→2)-α-D-Man*p*-OMe. As is evident from Figure 1, the two ROA spectra are very similar, which indicates that the conformation of some of the glycan chains of glycoproteins may directly be deduced from the ROA spectra. In the case of invertase, the main contribution to the ROA spectrum originates from the α-(1→2)-linked mannose parts of the glycans. The similarities in the ROA spectra also strongly suggest that the conformation of the trisaccharide in solution is very similar to the conformation of this unit in the glycans.

CP1267, *XXII International Conference on Raman Spectroscopy*
edited by P. M. Champion and L. D. Ziegler

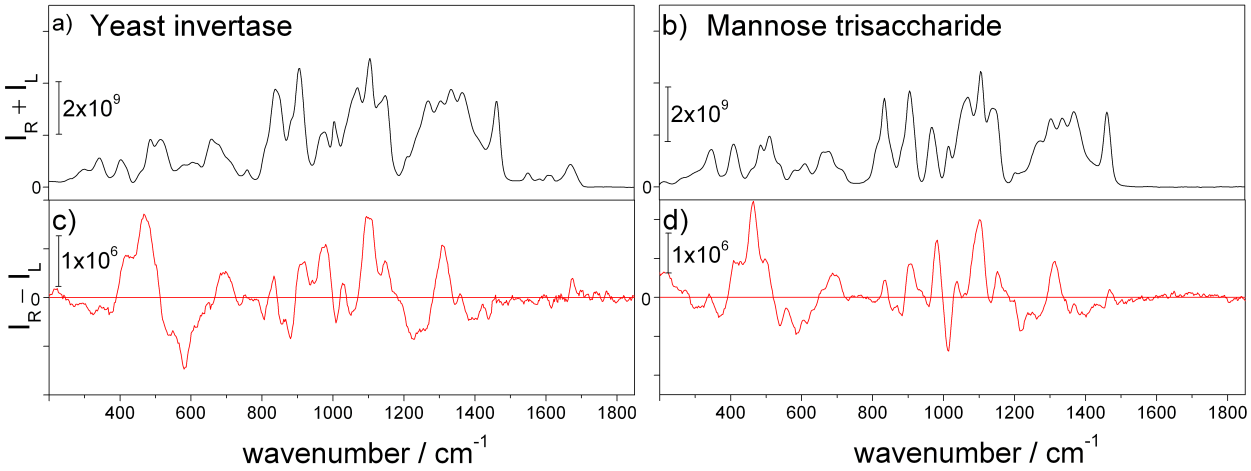

FIGURE 1. Experimental Raman (a,b) and ROA (c,d) spectra of yeast invertase (a,c) and the trisaccharide α-D-Man*p*-(1→2)-α-D-Man*p*-(1→2)-α-D-Man*p*-OMe (b,d). The similarity of the spectra implies similar carbohydrate conformation and little or no secondary protein structure.

The study of conformational elements in glycoprotein sugar moieties consequently appears to be possible, both experimentally by synthesizing and measuring ROA of smaller carbohydrate units with unique anomeric distribution and glycosidic linkage type, and theoretically by modeling molecules of equal size. In addition to the results presented above, the ROA contributions of α-(1→3)-linked mannose saccharides and mixed α-(1→2) and α-(1→3) type compounds are examined, based on a combination of experimental and predicted ROA spectra. The importance of conformational sampling in the theoretical studies of carbohydrates will also be briefly discussed.

ACKNOWLEDGMENTS

The Glasgow authors acknowledge the EPSRC for funding. This work was supported by grants from the Swedish Research Council (VR) and The Knut and Alice Wallenberg Foundation.

REFERENCES

1. L.D. Barron, F. Zhu, L. Hecht, G.E. Tranter and N.W. Isaacs, *J. Mol. Struc.* **834-836**, 7-16 (2007).
2. K. Ruud, T. Helgaker and P. Bour, *J. Phys. Chem. A* **106**, 7448-7455 (2002).
3. O. Quinet, V. Liégeois, and B. Champagne, *J. Chem. Theory Comput.* **1**, 444-452 (2005).
4. V. Liégeois, K. Ruud and B. Champagne, *J. Chem. Phys.* **127**, 204105 (2007).
5. M. Pecul, *Chirality*, **21**, E98-E104 (2009).
6. BioTools Inc. Jupiter FL. Home page: www.btools.com.
7. F. Zhu, J. Kapitan, G.E. Tranter, P.D.A. Pudley, N.W. Isaacs, L. Hecht and L.D. Barron, *Proteins* **70**, 823-833 (2008).
8. C. Johannessen, J. Kapitan, H. Collet, A. Commeyras, L. Hecht and L.D. Barron, *Biomacromolecules* **10**, 1662-1664 (2009).
9. C.R. Jacob, S. Luber and M. Reiher, *Chem. Eur. J.* **15**, 13491-13508 (2009).
10. Gaussian 09, Revision A.02, M.J. Frisch *et al.*, Gaussian Inc., Wallingford CT (2009).
11. DALTON, a molecular electronic structure program, Release 2.0 (2005), see http://www.kjemi.uio.no/software/dalton/dalton.html
12. F. Zhu, N.W. Isaacs, L. Hecht, G.E. Tranter and L.D. Barron, *Chirality* **18**, 103-115 (2006).