Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 8451–8453

Tetrahedron Letters

A characteristic CH band in VCD of methyl glycosidic carbohydrates

Tohru Taniguchi,[a] Kenji Monde,[a,*] Nobuaki Miura[a] and Shin-Ichiro Nishimura[a,b]

[a]*Laboratory for Bio-Macromolecular Chemistry, Division of Biological Sciences, Graduate School of Science, Frontier Research Center for Post-genomic Science and Technology, Hokkaido University, Kita-ku, Sapporo 001-0021, Japan*
[b]*National Institute of Advanced Industrial Science and Technology (AIST), Toyohira-ku, Sapporo 062-8517, Japan*

Received 20 August 2004; revised 13 September 2004; accepted 15 September 2004

Abstract—Novel vibrational circular dichroism (VCD) studies in the CH region of a series of methyl glycosidic carbohydrates were examined. The specific CH stretching VCD band predicts absolute stereochemistries of their anomeric positions. The C-1 chiral information was extracted to the methoxy substituent as a probe. The concept of the vibrational chirality probe from a single chiral center in the presence of numerous such centers might be useful in determining the absolute configuration, when a multiplicity of chiral centers is present in a molecule such as a carbohydrate.

Chiral molecules exhibit circular dichroism (CD), the differential absorption of left versus right circularly polarized light, and CD spectroscopies have been useful for determining absolute configurations. Recently, measurement of CD in the infrared region, that is, vibrational circular dichroism (VCD),[1] has been advanced instrumentally and theoretically. VCD has some advantages over conventional electronic circular dichroism (ECD) due to the applicability to all organic molecules and the reliability of ab initio quantum calculation. However, for a molecule with many chiral centers, determination of the absolute configuration tends to be difficult because the information from each stereochemical center is mixed and averaged over the spectrum.

In our chiral analysis studies,[2] we applied VCD spectroscopy to carbohydrates. Carbohydrates are composed of multiple chiral centers, but currently most carbohydrate analyses are based on achiral methods such as NMR or MS spectroscopies, and chiral approaches are limited to a few techniques such as optical rotation or ECD.[3] All carbohydrates absorb IR and thus VCD spectroscopy should be capable of extracting detailed stereochemical information on carbohydrates. However, only a few carbohydrate VCD studies have been reported to date.[4] We have been constructing an extensive carbohydrate VCD database for the mid-IR region, with the aim of creating a novel methodology for carbohydrate analysis.[5] Recently, we reported an α-glycoside characteristic band, the glycoside band, which was observed around 1145 cm^{-1}.[6] This result showed the effectiveness of VCD over other spectroscopies for the determination of stereochemistry in carbohydrates and indicated that detailed carbohydrate VCD studies should be possible in the CH stretching region as well as in the mid-IR region. In the CH stretching region, only two VCD studies on carbohydrates have been reported,[4a,c] and spectra–structure correlation, as determined for the glycoside band, remains to be investigated. In this paper, we report that methyl glycosides exhibit a characteristic VCD peak, the sign of which solely reflects the C-1 absolute configuration.

Methyl α-L-arabinopyranoside was synthesized using Fischer glycosidation of L-arabinose and methanol and the resulting anomers were separated using HPLC. Methyl-d_3 α- and β-D-glucopyranosides were synthesized in a similar manner using D-glucose and methanol-d_4. The other methyl glycopyranosides were purchased and measured without further purification except for methyl β-D-mannopyranoside, which was measured after twice being evaporated from methanol. IR and VCD spectra were measured at 4 cm^{-1} resolutions using a JASCO FT/IR-470 spectrometer (16 scans) and a JASCO

Keywords: VCD; CH stretching region; Carbohydrate; Methyl glycoside; Vibrational chirality probe.

* Corresponding author. Tel.: +81 11 706 9041; fax: +81 11 706 9042; e-mail: kmonde@glyco.sci.hokudai.ac.jp

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.09.108

JV-2001 spectrometer with an InSb detector (20,000 scans), respectively. DMSO-d_6 was selected as a solvent for its strong solubility and nonabsorption in the region of interest. All spectra were recorded in a CaF_2 cell with a 50 μm pathlength at a concentration of 0.64 M.

Figure 1 shows the VCD spectra of α- and β-stereoisomers of the methyl pyranosides of D-glucose, D-galactose, D-mannose, D-xylose, L-arabinose, and L-fucose. In the CH stretching region, a reversal of the absolute configuration at a single chiral center could strikingly change the VCD spectral pattern, as was observed for some monosaccharides in the mid-IR region. Moreover, we noticed that the VCD band near 2840 cm^{-1} showed a positive sign for the *R*-configuration at C-1 (the α-anomers for D-sugars and the β-anomers for L-sugars) and a negative sign for the *S*-configuration. Previously, the IR band around 2840 cm^{-1} of methyl glucopyranoside was assigned as the symmetric methyl stretching motion.[7] Thus, this characteristic VCD band could be assigned to the symmetric methyl stretching vibration. This was confirmed by the measurement of the VCD spectra of methyl-d_3 D-glucopyranosides, in which the VCD band as well as the IR band at around 2840 cm^{-1} disappeared (Fig. 2). These results indicate that the anomeric configuration of these sugars can be

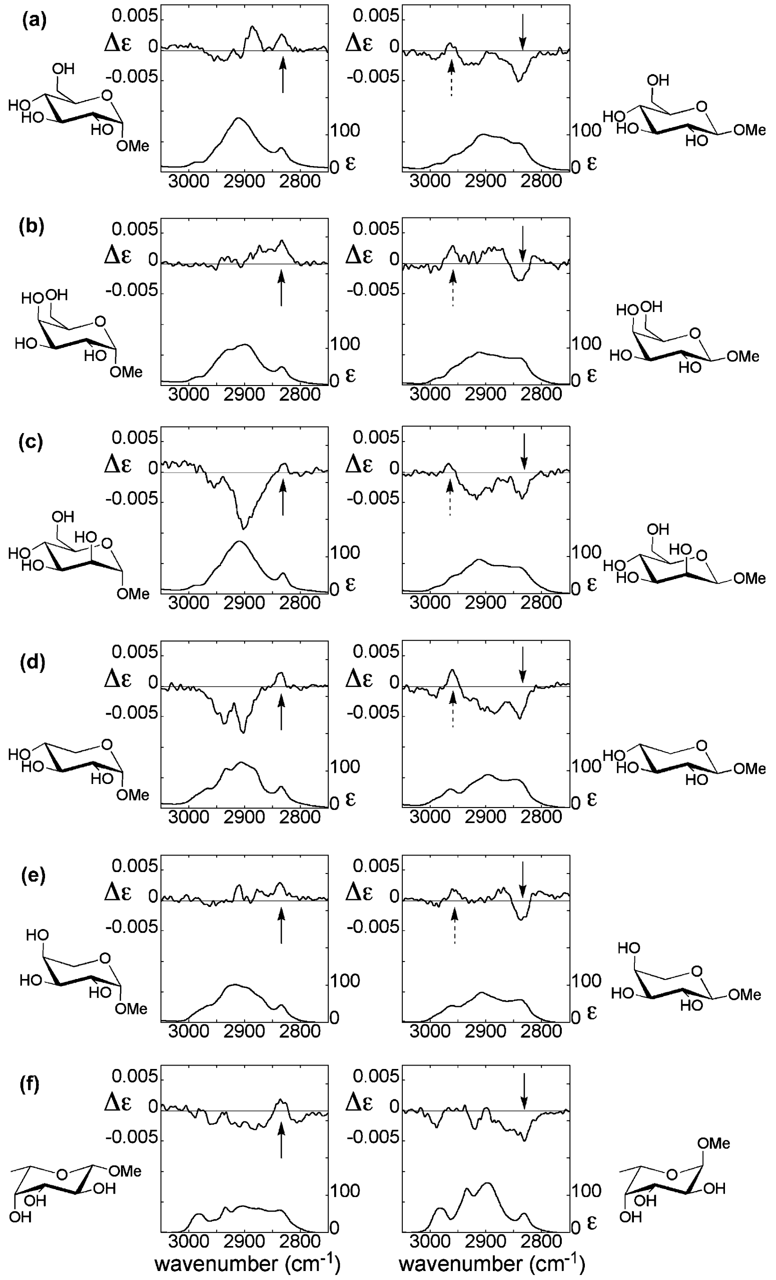

Figure 1. VCD and IR spectra of (a) methyl D-glucopyranoside, (b) methyl D-galactopyranoside, (c) methyl D-mannopyranoside, (d) methyl D-xylopyranoside, (e) methyl L-arabinopyranoside, and (f) methyl L-fucopyranoside. The anomers with *R*-configuration at C-1 (the α-anomer for D-sugars and the β-anomer for L-sugars) are in the left column, and those with *S*-configuration at C-1 (the β-anomer for D-sugars and the α-anomer for L-sugars) are in the right column. The solid arrows and the dotted arrows indicate the symmetric methyl stretching and the asymmetric methyl stretching VCD bands, respectively.

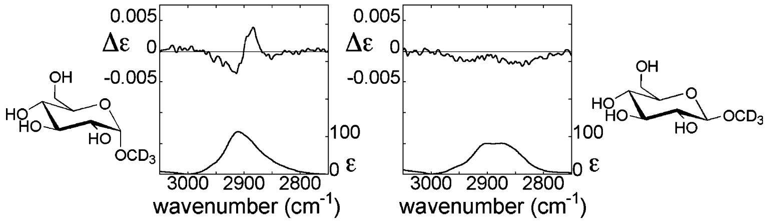

Figure 2. VCD and IR spectra of methyl-d_3 α-D-glucopyranoside (left) and methyl-d_3 β-D-glucopyranoside (right).

predicted by simply comparing the sign of this VCD band.[8] A positive peak with moderate intensity appeared at ~2960 cm^{-1} for the *S* series with the exception of methyl L-fucopyranoside, while *R* series did not show. This peak, designated as the asymmetric methyl stretching vibration,[7] is another possible means to distinguish the anomeric configuration.

The VCD feature of the symmetric methyl stretching motion reflects only the anomeric stereochemistry, with peaks simply displaying the opposite sign for the reversal of C-1 configuration. Therefore, the chirality of the CH VCD band can be considered to be result predominantly from the single anomeric chiral center, in spite of a multiplicity of chiral centers in the molecule. That is, the methoxy group serves as a probe to extract C-1 stereochemical information. Other substituents could be utilized in the same way, such as the acetate group, which has been suggested as a useful stereochemical probe due to its highly isolated C=O absorption.[4f] This concept implies that chiral information at the other positions could be extracted into a vibrational mode such as the symmetric methyl stretching or C=O stretching mode, achieved through simple selective modification to the hydroxyl group(s) of interest.

In conclusion, we identified a specific VCD band representing the absolute stereochemistry of a single asymmetric center. Namely, the C-1 chiral information was extracted in the methoxy substituent as a probe. The concept of the vibrational chirality probe from a single chiral center in the presence of numerous such centers might be helpful in determining the absolute configuration. Since theoretical VCD calculation for a large or flexible molecule is generally difficult, this approach could be particularly useful for such molecules, including carbohydrates.

Acknowledgements

This research was supported in part by a Grant-in-Aid for scientific research (Grants 14658181, 16310144) and by a National Project on Functional Glycoconjugate Research Aimed at Developing for a New Industry from the Ministry of Education, Science, Sports, and Culture of Japan.

References and notes

1. (a) Dukor, R. K.; Nafie, L. A. Vibrational Optical Activity of Pharmaceuticals and Biomolecules. In *Encyclopedia of Analytical Chemistry*; Meyers, R. A., Ed.; John Wiley & Sons: Chichester, 2000; pp 662–676; (b) Nafie, L. A.; Freedman, T. B. Vibrational Optical Activity Theory. In *Circular Dichroism: Principles and Applications*; Berova, N., Nakanishi, K., Woody, R. W., Eds., 2nd ed.; Wiley-VCH: New York, 2000; pp 97–131; (c) Freedman, T. B.; Cao, X.; Dukor, R. K.; Nafie, L. A. *Chirality* **2003**, *15*, 743–758.
2. Monde, K.; Taniguchi, T.; Miura, N.; Nishimura, S.-I.; Harada, N.; Dukor, R. K.; Nafie, L. A. *Tetrahedron Lett.* **2003**, *44*, 6017–6020.
3. Berova, N.; Nakanishi, K. The Exciton Chirality Method. In *Circular Dichroism: Principles and Applications*; Nakanishi, K., Berova, N., Woody, R. W., Eds.; Wiley-VCH: New York, 1994; pp 361–398.
4. (a) Marcott, C.; Havel, H. A.; Overend, J.; Moscowitz, A. *J. Am. Chem. Soc.* **1978**, *100*, 7088–7089; (b) Back, D. M.; Polavarapu, P. L. *Carbohydr. Res.* **1984**, *133*, 163–167; (c) Paterlini, M. G.; Freedman, T. B.; Nafie, L. A. *J. Am. Chem. Soc.* **1986**, *108*, 1389–1397; (d) Bose, P. K.; Polavarapu, P. L. *Carbohydr. Res.* **1999**, *319*, 172–183; (e) Bose, P. K.; Polavarapu, P. L. *J. Am. Chem. Soc.* **1999**, *121*, 6094–6095; (f) Bose, P. K.; Polavarapu, P. L. *Carbohydr. Res.* **1999**, *322*, 135–141.
5. Taniguchi, T.; Miura, N.; Nishimura, S.-I.; Monde, K. *Mol. Nutr. Food Res.* **2004**, *48*, 246–254.
6. Monde, K.; Taniguchi, T.; Miura, N.; Nishimura, S.-I. *J. Am. Chem. Soc.* **2004**, *126*, 9496–9497.
7. (a) Socrates, G. *Infrared and Raman Characteristic Group Frequencies*, 3rd ed.; John Wiley & Sons: Chichester, 2001; pp 50–67; (b) Nakanishi, K.; Solomon, P. H. *Infrared Absorption Spectroscopy*, 2nd ed.; Boca Raton: Emerson-Adams Press, 1977; pp 185–186.
8. Methyl α- and β-D-glucopyranosides were previously noted to exhibit approximate mirror images throughout the CH stretching region, accidentally.[4a]