ARTICLE

Deuterium Labelling to Extract Local Stereochemical Information by VCD Spectroscopy in C-D Stretching Region: A Case Study of Sugars

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Mohamad Zarif Mohd Zubir,†[a] Nurul Fajry Maulida,†[a] Yoshihiro Abe,[a] Yuta Nakamura,[a] Mariam Abdelrasoul,[a,c] Tohru Taniguchi*[b] and Kenji Monde*[b]

Stereochemical elucidation of molecules with multiple chiral centers is difficult. Even with VCD spectroscopy, excluding all but one diastereomeric structural candidates is challenging because stereochemical inversion of one chiral center among many centers does not always result in noticeable differences in their VCD spectra. This work demonstrates that introduction of a suitable VCD chromophore with absorption in the 2300-1900 cm^{-1} region can be used for extracting local stereochemical information and for stereochemical assignment of C-1 of various sugars as a case study. Through studies on a series of epimeric pairs of monosaccharides and their derivatives, we found that the introduction of one -OCD_3 group to each C-1 position produced almost mirror-image VCD patterns in the 2300-1900 cm^{-1} region depending on the C-1 stereochemistry irrespective of the other molecular moiety. This work also shows that comparison of the observed VCD signals in this spectral region and calculated ones enables the stereochemical assignment of a chiral center in the vicinity of the chromophore. This study provides a proof of concept that the use of a VCD chromophore in the 2300-1900 cm^{-1} region enables the analysis of selected stereochemistry of suitable molecular systems. Further studies on this concept should lead to development of a method useful for the structural elucidation of other types of complex molecules.

Introduction

Middle-sized natural products (M.W. 500 to 2,000) such as oligosaccharides, cyclic peptides, macrolides, and other metabolites are promising drug candidates beyond Lipinski's rule of 5. Because middle-sized molecules target, for example, protein-protein interactions more efficiently than small molecules do, a large number of such drugs have been approved and under development in recent years. [1, 2] For exploration of such natural products and their synthetic derivatives, their structural elucidation is one of the major bottlenecks as they possess multiple chiral centers. NMR coupling analysis and 2D NMR may establish the atom connectivity. However, such traditional analysis usually does not exclude all but one diastereomeric structural candidates. As a result, multiple analytical methods (e.g., Mosher-Kusumi method,[3] NMR DP4 analysis,[4] electronic circular dichroism spectroscopy,[5, 6] vibrational circular dichroism (VCD) spectroscopy,[6-9] Raman optical activity (ROA) spectroscopy,[7, 8] and chemical correlation) are applied to elucidate the stereochemistry of as many chiral centers in target molecules as possible.[10-12] Crystallization of middle-sized molecules suited for structural analysis by X-ray crystallography is not tedious. Crystalline sponge method[13] and cryoEM method microED[14] are emerging powerful analysis techniques for small organic molecules, but their applicability to middle-sized, flexible molecules are yet to be studied. New analytical methods that complement existing ones should facilitate studies involving middle-sized molecules.

VCD spectroscopy has become one of the most used methods to assign the absolute configuration of natural products and their synthetic derivatives.[6-9] Stereochemical elucidation of molecules with more than one chiral center is possible, as diastereomers of small molecules often show satisfactorily different VCD patterns.[15-18] Since VCD signals originate from vibrational transitions, functional groups in the vicinity of the chiral center of interest tend to show characteristic signals that is indicative of its stereochemistry. For example, Merten and coworkers reported that some of anthrone and oxanthrone glucosides show characteristic VCD signals in the 1650-1500 cm^{-1} region that may serve as a marker for the configuration of the C-10 stereocenter.[19] Herrebout, Batista Jr. and coworkers suggested that spectral patterns at around 1390 cm^{-1} observed for acetonized 1,3-diols are markers for the absolute configuration of *syn*- and *anti*-oriented hydroxyl groups.[20] Such spectra-structures relationships provide useful criteria to assign diastereomeric structures of small molecules. However, spectral differences may be

[a] *Graduate School of Life Science, Hokkaido University, Kita 21 Nishi 11, Sapporo 001-0021, Japan*
[b] *Frontier Research Center for Advanced Material and Life Science, Faculty of Advanced Life Science, Hokkaido University, Kita 21 Nishi 11, Sapporo 001-0021, Japan*
[c] *Department of Medicinal Chemistry, Faculty of Pharmacy, Assiut University, Assiut 71526, Egypt*
† Equal contribution.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

obscured for multi-functionalized middle-size molecules with many chiral centers, as reversal of a single chiral center (an epimer) may not produce a noticeable spectral change. This point was also discussed by Reiher and coworkers in their studies on the limitation of ROA spectroscopy to distinguish molecules with many chiral centers.[21]

Common organic molecules do not show strong absorption in the 2300-1900 cm^{-1} region. Use of VCD spectroscopy in this region is a promising approach to extract stereochemical information from middle-sized molecules. In continuation of our studies on VCD couplet,[22-25] we recently showed that interaction of two azido groups produce a strong VCD couplet (at ca. 2100 cm^{-1}) whose shape depends on the local environment around the azido groups.[26] Although this finding should be useful in the analysis of, for example, the conformation of biomolecules, the necessity of introducing two azido groups to suitable positions limits its application to multi-functionalized middle-sized molecules. If one chromophore, not two, in the 2300-1900 cm^{-1} region is found sufficient to extract local stereochemical information and if the resultant VCD pattern is predictable by theoretical calculations, these should pave a way to develop new methods to elucidate the selected stereochemistry of target molecules. To prove this concept, one needs to prepare a series of diastereomeric pairs with a suitable VCD chromophore and confirm that their VCD spectra in the 2300-1900 cm^{-1} region exhibit drastically different, ideally mirror-image, patterns irrespective of the other chiral centers. To provide a proof of concept, this work studied a methoxy-d_3 group (-OCD_3) installed at the C-1 position of a series of mono- and disaccharides and their derivatives. Sugars are chosen as a model system because of their diverse stereochemistry and functional groups, but we hope to apply the concept proven here to other types of molecules in future studies. Herein, we show the feasibility of the concept to determine the absolute configuration of the chiral center in the vicinity of an introduced chromophore, in this case study the C-1 stereochemistry of sugars, by VCD spectroscopy in the 2300-1900 cm^{-1} region.

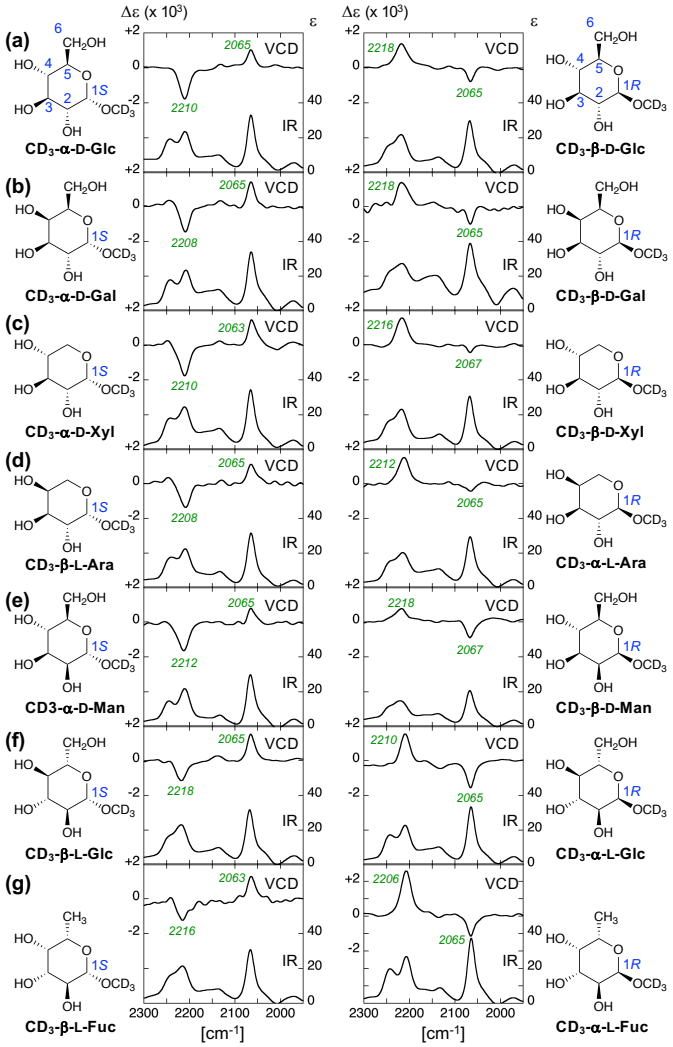

Fig. 1. Structures and observed VCD and IR spectra of methyl-d_3 glycopyranosides derived from (a) D-glucose, (b) D-galactose, (c) D-xylose, (d) L-arabinose, (e) D-mannose, (f) L-glucose, and (g) L-fucose with (left) 1*S* configuration and (right) 1*R* configuration. Wavenumbers of VCD signal extrema for ν_s CD_3 (lower frequency) and ν_{as} CD_3 (higher frequency) are labelled in italic (green). Measurement conditions: *c* 0.5 – 2.0 M in DMSO-h_6, *l* 50 μm.

Results and discussion

We started with studying monosaccharides possessing a -OCD_3 group. Considering the biological abundance and importance, D-glucose (**D-Glc**) and its enantiomer (**L-Glc**), D-galactose (**D-Gal**), D-xylose (**D-Xyl**), L-arabinose (**L-Ara**), D-mannose (**D-Man**), and L-fucose (**L-Fuc**) were selected. For each epimeric pair of methyl-d_3 glycopyranosides, their C-1 configuration is denoted as α or β (Fig. 1).

Most of the methyl-d_3 glycopyranosides were synthesized by Fischer glycosidation to produce α-β mixtures (free monosaccharides in CD_3OD stirred with catalytic acid), benzoylation (to facilitate diastereoseparation), chromatographic separation, and deprotection of benzoyl groups. Sterically and stereoelectronically unfavoured β-mannoside **CD_3-β-D-Man** was synthesized with using Crich β-mannosylation.[27]

Obtained methyl-d_3 glycopyranosides were dissolved in DMSO-h_6 and placed in a 50-μm BaF_2 cell for VCD measurement in the 2300-1900 cm^{-1} region. Note that DMSO-h_6, not DMSO-d_6, was used because the latter shows strong solvent absorption in this region due to C-D stretching vibrations. Fig. 1a shows the VCD and IR spectra of **CD_3-α-D-Glc** and **CD_3-β-D-Glc**. For both epimers, two VCD bands were detected at 2065 cm^{-1} and around 2210 cm^{-1}. These signals were respectively assigned as symmetric (ν_s) and asymmetric (ν_{as}) CD_3 stretching vibrations.[28] To our surprise, these epimers showed almost mirror-image VCD patterns: **CD_3-α-D-Glc** showed a positive VCD signal for ν_s CD_3 and a negative one for ν_{as} CD_3, while **CD_3-β-D-Glc** showed a negative signal for ν_s CD_3 and a positive one for ν_{as} CD_3. It should be emphasized that such VCD patterns are exhibited despite the common presence of other four chiral centers (C2 to C5). Encouraged by this result, we studied the VCD of other monosaccharides. Changes in the configuration at C-4 did not affect the sign of the VCD signals of ν_s and ν_{as} CD_3 (Fig. 1b). Loss

of the hydroxymethyl group at C-5 resulted in the reduction of the intensity of the ν_s CD_3 signal for the 1*S* series (**CD_3-α-D-Man** and **CD_3-β-L-Ara**) but maintained the overall sign patterns (Fig. 1c and d). Reversal of the C-2 configuration also did not change the sign pattern for both 1*S* and 1*R* epimers (Fig. 1e). Stereochemical inversions of C-3 and C-5 as well as the substitution of C-5 hydroxymethyl to methyl group were also tolerated (Fig. 1f and g). For all the tested monosaccharides in Fig. 1, the 1*S* epimers showed a positive VCD signal for ν_s CD_3 and a negative one for ν_{as} CD_3, whereas the 1*R* epimers showed a negative signal for ν_s CD_3 and a positive one for ν_{as} CD_3. Thus, C-1 epimeric pairs exhibited mirror-image VCD patterns irrespective of the changes in the configurations and substituents at other positions. This indicated that extraction of the stereochemical information of a selected site from molecules with multiple chiral centers is possible for suitable cases with the use of a suitable VCD chromophore in the 2300-1900 cm^{-1} region.

Next, we tested the feasibility of determining the stereochemistry at C-1 solely by comparison of the observed CD_3 VCD signals and calculated signals in the 2300-1900 cm^{-1} region. VCD spectra of representative **CD_3-α-D-Glc** and **CD_3-β-D-Glc** were calculated at the B3LYP/6-31G(d) level of theory with or without using polarizable continuum model (PCM) for DMSO. Both gas phase and PCM(DMSO) conditions predicted similar VCD spectra for each molecule (Fig. 2a). Importantly, these spectra well reproduced the observed CD_3 VCD patterns: **CD_3-α-D-Glc** showed a positive signal for ν_s CD_3 and a negative one for ν_{as} CD_3, whereas **CD_3-β-D-Glc** showed a negative signal for ν_s CD_3 and a positive one for ν_{as} CD_3. These results proved it feasible to determine the stereochemistry of a chiral center in the vicinity of a VCD chromophore in 2300-1900 cm^{-1} with using theoretical VCD calculations.

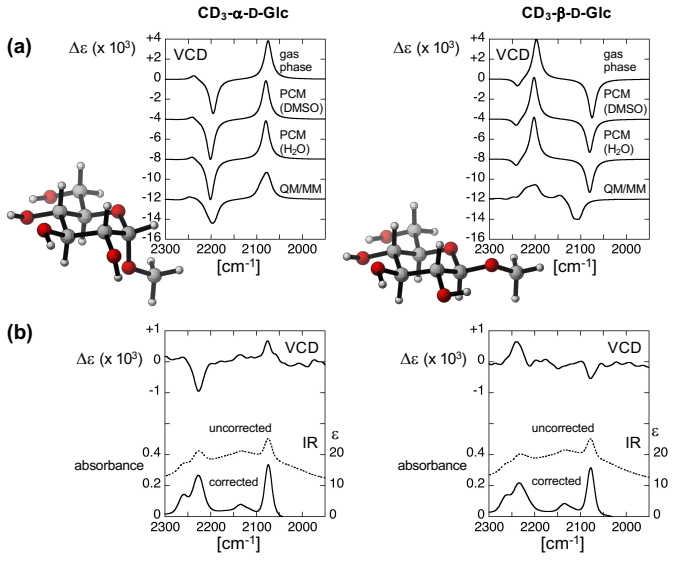

Fig. 2. Calculated VCD spectra using several conditions and observed VCD/IR spectra for H_2O solution of **CD_3-α-D-Glc** (left) and **CD_3-β-D-Glc** (right). (a) VCD spectra predicted in the gas phase, with PCM for DMSO, with PCM for water, and with explicit water molecules. The most stable conformers predicted using PCM for water are drawn. DFT calculation conditions: B3LYP/6-31G(d) with or without PCM. See Supplementary Information for QM/MM calculation conditions. Frequency scaling factor: 0.955 for all the calculated spectra. (b) Observed VCD spectra corrected by a solvent VCD spectrum in Δε, uncorrected raw IR spectra in absorbance, and observed IR spectra corrected by a solvent IR spectrum in ε. Measurement conditions: *c* 3.0 M in H_2O, *l* 25 μm.

Chromophores in the 2300-1900 cm^{-1} region are advantageous for studying hydrophilic biomolecules. VCD measurements of H_2O solutions below 1900 cm^{-1} must be carried out in a special sample cell with a short pathlength (10 μm or shorter) and accordingly at very high sample concentration to circumvent its strong solvent absorption. With H_2O less absorbing in the 2300-1900 cm^{-1} region, VCD study in this region can be performed with a longer pathlength and a slightly lower concentration. Fig. 2b shows the VCD spectra of H_2O solutions of **CD_3-α-** and **β-D-Glc** in a 25-μm CaF_2 cell. These VCD showed the same sign patterns to those observed for the DMSO-h_6 solutions. The observed VCD spectra in H_2O also were well reproduced by DFT calculations with implicit (PCM) as well as explicit (two-layer quantum mechanics (QM)/ molecular mechanics (MM) method for several MD snapshots with ca. 120 water molecules) models for H_2O (Fig. 2a and Fig. S1). While -OCD_3 group is promising for

While we initiated this work with the hope of seeing enough spectral differences for distinguishing epimers, such mirror-image patterns ideal for stereochemical assignment were far better than expected. In many reported cases, chromophores in a pair of epimers do not always produce mirror-image VCD signals due to influences from the rest of the molecule.[15-18, 20] Minor perturbation to the CD_3 VCD signals may be ascribed to the highly localized vibrational nature of the ν_s and ν_{as} CD_3 modes, as found for calculated **CD_3-α-** and **β-D-Glc** (Fig. S2). Independence of these CD_3 vibrations were also bolstered by theoretical calculations of methyl-d_3 glycopyranosides without substituents at C2-5 positions (models (*S*)-**1** and (*R*)-**1**). Theoretical VCD spectra of (*S*)-**1** and (*R*)-**1** exhibited the same VCD sign patterns as those observed for 1*S* and 1*R* series of monosaccharides, respectively (Fig. 3). Moreover, CD_3 VCD signals were less affected by conformational differences. Pyranose ring in sugars is known to take two main chair conformations $^4C_1$ and $^1C_4$. The -OCD_3 group is oriented either axial or equatorial depending on the ring conformation. Inspection of the VCD spectra in Fig. 2 and the preferred chair conformations of these monosaccharides (Fig. S3) suggested that the CD_3 VCD sign patterns were consistent for both the axially- and equatorially-oriented -OCD_3 groups. The consistency of the VCD sign patterns was also found for calculated spectra of both the $^4C_1$ and $^1C_4$ conformers of (*S*)- and (*R*)-**1** (Fig. 3). Last, use of less polar solvent also yielded the same sign patterns. See Fig. S4 for the VCD spectra of **CD_3-α-D-Bz$_4$G**, **CD_3-β-D-Bz$_4$G**, **CD_3-α-D-6LG**, and **CD_3-β-D-6LG** (vide infra) in $CHCl_3$. Other samples studied here could not be dissolved in apolar solvents. Overall, these results revealed the highly independent nature of the CD_3 VCD signals from other part of the molecule, which gave rise to almost mirror-image VCD patterns between epimers. Although whether mirror-image patterns are seen for other chromophores and other molecular systems is yet to be studied, these results suggested the importance of isolated vibrational modes for application of this concept for other molecules. It should also be noted that

similarity between the VCD features of experimental **CD₃-α-** and **β-D-Glc** and those of computational (*S*)- and (*R*)-**1** indicates the possibility of using an extremely simplified structure for calculations.

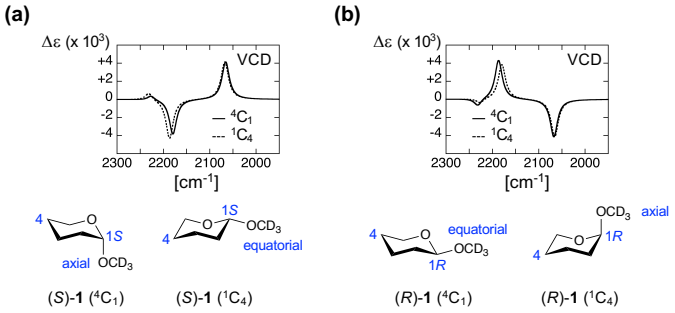

Fig. 3. Calculated VCD spectra of simplified models (a) (*S*)-**1** and (b) (*R*)-**1** in $^4C_1$ and $^1C_4$ conformations. Calculation conditions: DFT/B3LYP/6-31G(d). Frequency scaling factor: 0.955 for all the spectra.

To showcase the wide applicability of the concept of extraction of local stereochemical information by -OCD_3 group, we studied the VCD spectra of the C-1 epimeric pairs of D-gentiobiose (β1,6-linked glucose dimer, **D-Gen**), 5-membered D-glucofuranoside (**D-*f*Glc**), and 2,3,4,6-*O*-tetrabenzoylated D-glucopyranoside (**D-Bz₄G**) (Fig. 4a-c). **CD₃-α-D-Gen** was synthesized starting from **CD₃-α-D-Glc** with using Kahne sulfoxide glycosylation,[29] whereas **CD₃-β-D-Gen** was prepared from D-gentiobiose by a 3-step synthesis. Meanwhile, **CD₃-α-** and **β-D-*f*Glc** were obtained by $FeCl_3$-mediated glycosidation of D-glucose.[30] **D-Bz₄G** epimers are synthetic intermediates of **CD₃-α-** and **β-D-Glc**. Their VCD spectra in DMSO-h_6 are shown in Fig. 4a-c. All the α epimers (1*S* series) showed a positive ν_s CD_3 signal and a negative ν_{as} CD_3 one, whereas β (1*R*) counterparts showed the opposite pattern. Thus, their OCD_3 VCD signals well reflected the stereochemistry of interest even for a disaccharide with 10 chiral centers, a sugar with a different ring size, and a multi-chromophoric larger molecule. These results highlighted the potential of the concept of stereochemical assignment of the selected site for larger, complex molecular systems.

Isotopically labelled molecules are processed by enzymes often equally as their non-labelled counterparts. This permits biochemical utility of deuterium-containing chromophores for sample preparation and for tracking the stereochemical outcome of reactions. Such applications were demonstrated in a study on an epimeric pair of 6-*O*-lauroylated D-glucose (**6LG**) (Fig. 4d). Non-labelled **CH₃-α-** and **β-6LG** are surfactant molecules with antimicrobial activity[31, 32] and have been prepared by lipase-catalyzed reactions from the corresponding **CH₃-α-** and **β-D-Glc**.[33] Following the procedure for the enzymatic conversion of methyl-h_3 species, we prepared **CD₃-α-** and **β-D-6LG** from **CD₃-α-** and **β-D-Glc**, respectively. The obtained lauroylated epimers showed VCD patterns well reflecting their C-1 stereochemistry (Fig. 4d). From the viewpoint of stereochemical tracking, VCD spectroscopy confirmed that the C-1 stereochemistry was unaffected before and after the enzymatic transformation. With the insight obtained in this work, applications of VCD spectroscopy in the 2300-1900 cm^{-1} region for monitoring a stereochemical outcome of enzymatic as well as chemical reactions for other classes of molecules should be possible in future. One of such applications is currently under study by our group.

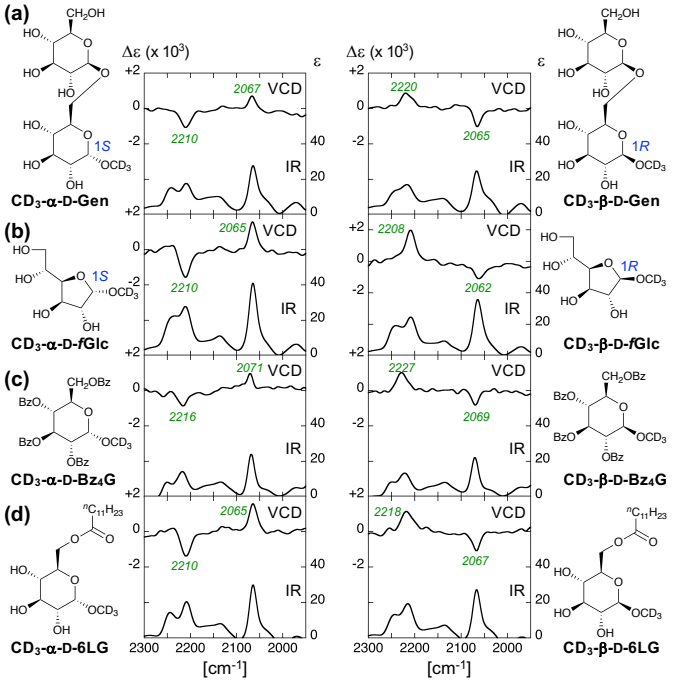

Fig. 4. Structures and observed VCD and IR spectra of methyl-d_3 glycosides derived from (a) D-gentiobiose, (b) D-glucofuranose, (c) 2,3,4,6-*O*-tetrabenzoyl-D-glucose, and (d) 6-*O*-lauroyl-D-glucose with (left) 1*S* configuration and (right) 1*R* configuration. Wavenumbers of VCD signal extrema for ν_s CD_3 (lower frequency) and ν_{as} CD_3 (higher frequency) are labelled in italic (green). Measurement conditions: *c* 0.5 or 1.0 M in DMSO-h_6, *l* 50 μm.

Conclusions

Stereochemical elucidation of multi-functionalized middle-sized molecules is difficult even with the use of several analysis methods. Through VCD studies on a series of methyl-d_3 glycoside, this work demonstrated that introduction of one VCD chromophore in the 2300-1900 cm^{-1} region enables extraction of local stereochemical information and determination of the stereochemistry of the chiral center of interest. Deuterium-containing VCD chromophores should be versatile when biochemical studies are involved. Although this work provided a proof of concept through studies on sugar molecules and -OCD_3 group, the insight obtained here should facilitate the structural elucidation of other types of complex molecules in combination with other analytical methods.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by KAKENHI Grant Nos. JP18H02093, JP18KK0394, and JP19H02836. M. Z. M. Z. is grateful for a scholarship from International Graduate Program (IGP), Hokkaido University. N. F. M. acknowledges Indonesian Endowment Fund for Education (LPDP) scholarship. We thank Instrumental Analysis Division, Global Facility Center, Creative Research Institution, Hokkaido University for HRMS analysis.

Notes and references

1. Bradley C. Doak, B. Over, F. Giordanetto and J. Kihlberg, *Chemistry & Biology*, 2014, **21**, 1115-1142.
2. V. Poongavanam, B. C. Doak and J. Kihlberg, *Current Opinion in Chemical Biology*, 2018, **44**, 23-29.
3. I. Ohtani, T. Kusumi, Y. Kashman and H. Kakisawa, *Journal of the American Chemical Society*, 1991, **113**, 4092-4096.
4. S. G. Smith and J. M. Goodman, *Journal of the American Chemical Society*, 2010, **132**, 12946-12959.
5. N. Harada and K. Nakanishi, *Journal of the American Chemical Society*, 1969, **91**, 3989-3991.
6. A. Mándi and T. Kurtán, *Natural Product Reports*, 2019, **36**, 889-918.
7. P. L. Polavarapu and E. Santoro, *Natural Product Reports*, 2020, **37**, 1661-1699.
8. J. M. Batista, E. W. Blanch and V. D. Bolzani, *Natural Product Reports*, 2015, **32**, 1280-1302.
9. C. Merten, T. P. Golub and N. M. Kreienborg, *Journal of Organic Chemistry*, 2019, **84**, 8797-8814.
10. E. De Gussem, W. Herrebout, S. Specklin, C. Meyer, J. Cossy and P. Bultinck, *Chem-Eur J*, 2014, **20**, 17385-17394.
11. S. Tanaka, Y. Honmura, S. Uesugi, E. Fukushi, K. Tanaka, H. Maeda, K.-i. Kimura, T. Nehira and M. Hashimoto, *The Journal of Organic Chemistry*, 2017, **82**, 5574-5582.
12. Y. Morishita, H. Zhang, T. Taniguchi, K. Mori and T. Asai, *Organic Letters*, 2019, **21**, 4788-4792.
13. Y. Inokuma, S. Yoshioka, J. Ariyoshi, T. Arai, Y. Hitora, K. Takada, S. Matsunaga, K. Rissanen and M. Fujita, *Nature*, 2013, **495**, 461-466.
14. C. G. Jones, M. W. Martynowycz, J. Hattne, T. J. Fulton, B. M. Stoltz, J. A. Rodriguez, H. M. Nelson and T. Gonen, *ACS Central Science*, 2018, **4**, 1587-1592.
15. A. G. Petrovic, P. L. Polavarapu, J. Drabowicz, P. Łyżwa, M. Mikołajczyk, W. Wieczorek and A. Balińska, *The Journal of Organic Chemistry*, 2008, **73**, 3120-3129.
16. L. G. Felippe, J. M. Batista Jr, D. C. Baldoqui, I. R. Nascimento, M. J. Kato, Y. He, L. A. Nafie and M. Furlan, *Organic & Biomolecular Chemistry*, 2012, **10**, 4208-4214.
17. B. Gordillo-Román, J. Camacho-Ruiz, M. A. Bucio and P. Joseph-Nathan, *Chirality*, 2013, **25**, 939-951.
18. T. Taniguchi, K. Nakano, R. Baba and K. Monde, *Organic Letters*, 2017, **19**, 404-407.
19. D. P. Demarque, D. R. Pinho, N. P. Lopes and C. Merten, *Chirality*, 2018, **30**, 432-438.
20. F. Passareli, A. N. L. Batista, A. J. Cavalheiro, W. A. Herrebout and J. M. Batista, *Physical Chemistry Chemical Physics*, 2016, **18**, 30903-30906.
21. B. Simmen, T. Weymuth and M. Reiher, *The Journal of Physical Chemistry A*, 2012, **116**, 5410-5419.
22. T. Taniguchi and K. Monde, *Journal of the American Chemical Society*, 2012, **134**, 3695-3698.
23. T. Hongen, T. Taniguchi, S. Nomura, J. Kadokawa and K. Monde, *Macromolecules*, 2014, **47**, 5313-5319.
24. T. Taniguchi, D. Manai, M. Shibata, Y. Itabashi and K. Monde, *Journal of the American Chemical Society*, 2015, **137**, 12191-12194.
25. T. Taniguchi, *Bulletin of the Chemical Society of Japan*, 2017, **90**, 1005-1016.
26. T. Taniguchi, M. Z. M. Zubir, N. Harada and K. Monde, *Physical Chemistry Chemical Physics*, 2021, **23**, 27525-27532.
27. D. Crich, A. Banerjee and Q. Yao, *Journal of the American Chemical Society*, 2004, **126**, 14930-14934.
28. T. Taniguchi, K. Monde, N. Miura and S. Nishimura, *Tetrahedron Letters*, 2004, **45**, 8451-8453.
29. D. Kahne, S. Walker, Y. Cheng and D. Van Engen, *Journal of the American Chemical Society*, 1989, **111**, 6881-6882.
30. A. Lubineau and J.-C. Fischer, *Synthetic Communications*, 1991, **21**, 815-818.
31. T. Tamura, S. Shimizu, Y. Sasaki and C. Hirai, *Journal of Japan Oil Chemists' Society*, 1991, **40**, 321-325.
32. A. Smith, P. Nobmann, G. Henehan, P. Bourke and J. Dunne, *Carbohydrate Research*, 2008, **343**, 2557-2566.
33. J. Mutschler, T. Rausis, J.-M. Bourgeois, C. Bastian, D. Zufferey, I. V. Mohrenz and F. Fischer, *Green Chemistry*, 2009, **11**, 1793-1800.