Talanta 115 (2013) 870–875

Contents lists available at SciVerse ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Short communication

Differentiation of glucose-containing disaccharides isomers by fragmentation of the deprotonated non-covalent dimers using negative electrospray ionization tandem mass spectrometry

Debin Wan [a,b], Hongmei Yang [a], Cunyu Yan [c], Fengrui Song [a], Zhiqiang Liu [a], Shuying Liu [a,d,*]

[a] Changchun Center of Mass Spectrometry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, 5625 Renmin Street, Changchun 130022, China
[b] Graduate School of the Chinese Academy of Sciences, Beijing 100039, China
[c] Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing 100101, China
[d] Changchun University of Chinese Medicine, Changchun 130117, China

ARTICLE INFO

Article history:
Received 15 March 2013
Received in revised form
24 June 2013
Accepted 28 June 2013
Available online 9 July 2013

Keywords:
Disaccharide
Deprotonated dimer
Non-covalent complex
ESI-MS
Density functional theory

ABSTRACT

In this work, the glucose-containing disaccharide isomers were studied using negative electrospray ionization tandem mass spectrometry (ESI-MS/MS). Interestingly, the full-scan mass spectra of the disaccharides revealed that the deprotonated dimers were the predominant gas phase ions during ionization process. Importantly, several diagnostic fragment ions relative to linkage positions and anomeric configurations, arising from the covalent bond dissociation of dimers without breakdown of the non-covalent complexes, can be detected in the tandem mass spectra. Based on the scarce fragmentation characteristic, an original and simple approach for structural discrimination of disaccharide isomers was put forward. In addition, density functional theory (DFT) was employed to find out the reason why several fragmentations of intramolecular sugar bonds had preceded breakdown of the non-covalent complexes.

1. Introduction

Carbohydrates are ubiquitous compounds serving crucial structural and functional roles in almost all living organisms, and their structural elucidations are an essential prerequisite for understanding their many functions [1]. Carbohydrates are an extreme case of isomeric molecules, with 80–90% of carbons being chiral as well as having isomers with different positional linkage, and the amount of individual pure species is often severely limited. Therefore, a sensitive and effective analytical method for the structural determination of carbohydrate is required, which is still a great challenging task given to biochemists.

A combination of techniques such as NMR, methylation analysis (GC/MS), and monosaccharide composition analysis has long been a mainstay in carbohydrate chemistry [2,3]. With the development of soft ionization techniques, matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI) mass spectrometry (MS) [4,5], MS-based technology, in particular the ESI-tandem mass spectrometry (ESI-MS/MS), has become the key methodology for the analysis of underivatized carbohydrate both in the positive and negative ion modes, being sensitive and selective [6]. Positive- and negative- ion ESI-MS spectra could provide complementary information for the structural elucidation of oligosaccharides. In the positive ion mode, the dominant cross-ring cleavage ions concerning linkages derived from alkali metal attachment could be observed for the sugar unit at the reducing end [7,8]. In addition to sequence data, the fragmentation of negative ions could provide information on all linkage positions and anomeric configurations in the sugar chain [9–11]. However, the deprotonated ion signal of neutral carbohydrate in the negative ion mode has been proved to be much lower than that of sodium attachment ion in the positive ion mode. Furthermore, some fragment ions derived from the dissociation of deprotonated neutral carbohydrate can be detected in the full scan mass spectrum, rendering that the deprotonated ion is unstable [12,13]. To improve the signal intensity of neutral carbohydrate in negative ion mode, some frequent acid radicals should be added to form the anionic adducts necessarily, such as Cl^-, Br^-, I^-, F^-, CH_3COO^-, $HCOO^-$, NO_3^-, and $H_2PO_4^-$ [14,15]. Recently, carbohydrates have been found to be present as not only deprotonation and anion attachment but also the non-covalent sugar–sugar complex in the negative ion mode. It is because their adoptable structures allow them to have a range of potential hydrogen bonds,

* Corresponding author at: Chinese Academy of Sciences, Changchun Center of Mass Spectrometry, Changchun Institute of Applied Chemistry, 5625 Renmin Street, Changchun 130022, China. Tel.: +86 431 8526 2886.
E-mail addresses: syliu19@yahoo.com.cn, mslab11@ciac.jl.cn (S. Liu).

0039-9140/$ - see front matter Crown Copyright © 2013 Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.talanta.2013.06.055

attracting each other. Cotter's group investigated non-covalent sugar–sugar complexes by Infrared (IR) Atmospheric Pressure (AP) MALDI [16]. Interestingly, it was found that some fragmentation of intramolecular sugar bonds preceded the breakdown of the non-covalent complexes. It appeared that it happened only with sugars containing atleast one sialic acid, since the sialic acid has been proved to be a mediator in the non-covalent complex formation, associating tightly with other sugars. As for the neutral carbohydrates, similar noncovalent complexes had been observed, but only the breakdown of the noncovalent dimers could be detected by IR AP MALDI.

In the present research, the disaccharides were studied using negative ESI-MS/MS and one novel approximately symmetric non-covalent dimer of disaccharides had been detected to be stable and predominant, where the fragmentation was quiet different from the common non-covalent dimer of neutral carbohydrates. Apart from the fragment ions arising from the non-covalent bond dissociation of the dimers, other characteristic fragment ions from glycosidic cleavages and cross-ring product ions without the breakdown of non-covalent bond were observed in the tandem mass spectra. It may provide us a new approach to discriminate the native disaccharide isomers using tandem mass spectrometry. Most importantly, it is the first time that the fragmentation of intra-molecular sugar bonds without the breakdown of the non-covalent complex is discovered for the neutral carbohydrate.

2. Experimental

2.1. Reagents

Reducing neutral disaccharides as listed in Chart 1 are isomers of $C_{12}H_{22}O_{11}$ with four different linkage types (1-2, 1-3, 1-4, and 1-6) and two different anomeric configurations (α and β). D-glucose, sophorose, maltose, isomaltose, nigerose and sucrose (non-reducing disaccharide) were purchased from Sigma (St. Louis, MO, USA). Cellobiose and gentiobiose were bought from J&K (Beijing, China). Laminaribiose was acquired from Megazyme (Wicklow, Ireland). Kojibiose was acquired from Carbosynth (Berkshire, UK). Methanol used was of HPLC grade. HPLC grade deionized distilled water was obtained with a Milli-Q plus TOC water purification system (Millipore, Bedford, MA). The eight reducing disaccharide samples and non-reducing sucrose were prepared at a concentration of 10^{-4} mol/L in a solution of water/methanol (50/50, v/v).

2.2. Mass spectrometry

All mass spectra were recorded on an LTQ XL linear ion-trap mass spectrometer (Thermo Finningan, San Jose, CA, USA) equipped with an electrospray ionization source operated in negative ion mode. Samples were introduced at a flow rate of 5 μL/min. Typical ESI conditions were as follows: sheath gas flow 0.45 L/min and auxiliary gas flow 0.6 L/min (both nitrogen), spray voltage −4.0 kV, heated capillary temperature 300 °C, capillary voltage −20 V, and the tube lens offset −160 V. CID-MS/MS experiments were performed using standard isolation and excitation procedures (activation q value of 0.25; and activation time of 30 ms). Ions were isolated using a width of 2.0 m/z ($\pm$ 1.0 m/z). The relative collision energy was set at 10%. The rich structural information can be obtained under this condition. A total of 20–100 scans were accumulated for each spectral acquisition. Data acquisition was carried out with Xcalibur data system.

No.	Formula	Name
1	Glcα1-2Glc	Kojibiose
2	Glcβ1-2Glc	Sophorose
3	Glcα1-3Glc	Nigerose
4	Glcβ1-3Glc	Laminaribiose
5	Glcα1-4Glc	Maltose
6	Glcβ1-4Glc	Cellobiose
7	Glcα1-6Glc	Isomaltose
8	Glcβ1-6Glc	Gentiobiose

Chart 1. Reducing glucopyranosyl-glucose disaccharides.

2.3. Density function theory calculations

Theoretical methods were performed to calculate the geometric structures and intermolecular interaction energies of the studied system. The equilibrium structures of the neutral disaccharide, the deprotonanted disaccharide and the deprotonated disaccharide dimers were optimized by the density functional theory (DFT) level using the B3LYP functional and 6-31+G(d, p) basis set [17]. The intermolecular interaction energies were then calculated at B3LYP/6-31+G(d,p) level, since the missing diffuse functions were very important to quantitate electronic energies of anions correctly. Meanwhile, basis set superposition error (BSSE) using a counterpoise correction scheme was taken into account during the calculations for all dimer system at the level of B3LYP/6-31+G(d,p). All the calculations were performed using the Gaussian 09 software package.

3. Results and discussion

To obtain reproducible and high quality tandem mass spectra, the MS/MS experiments were carried out with the relative collision energy set at 10% to preserve the signal of the precursor ion in the range of 5–20%. The rich structural information can be obtained under this condition. The studied reducing disaccharides as listed in Chart 1 are isomers of $C_{12}H_{22}O_{11}$ with four different linkage types (1-2, 1-3, 1-4, and 1-6) and two different anomeric configurations (α and β). All the experiments were operated in the negative ion mode.

3.1. Mass spectrometric analysis of cellobiose

The results from negative ESI-MS analysis of disaccharides in this study were much different from previous reports [10,12,13]. Taking cellobiose as an example, the base peak in the negative full scan ESI-MS spectrum is the deprotonated dimer ion ($[2M-H]^-$) at m/z 683, rather than the deprotonated ion ($[M-H]^-$) at m/z 341, or the anion attachment ions such as $[M+HCOO]^-$ at m/z 387, $[M+Cl]^-$ at m/z 377, and $[M+C_3H_6O_3]^-$ at m/z 431, as depicted in Fig. 1a. Additionally, several ions (i. e. m/z 323, 263, 221 and 179) arising from the fragmentation of unstable deprotonated ion and other non-covalent complex ions at m/z 1025 ($[3M-H]^-$) and 1327 ($[4M-H]^-$) also can be observed. Even if the experiment was carried out using a different instrument, the dimer ion at m/z 683 could still be detected as long as it had been under the electrospray ion source (Fig. S-1 of Supporting information). Stemming from previous studies, it was noted that the noncovalent homodimers of sugars can be formed at high concentrations [18]. The dimers can be observed in a large range of sample concentration (10 μmol/L~1 mmol/L, Fig. S-2 of Supporting information). With the increase of the sample concentration, the propensity of the dimer formation would increase gradually. The dimer was formed without the loss of water or other small molecules indicated by its mass-to-charge ratio. Therefore, it

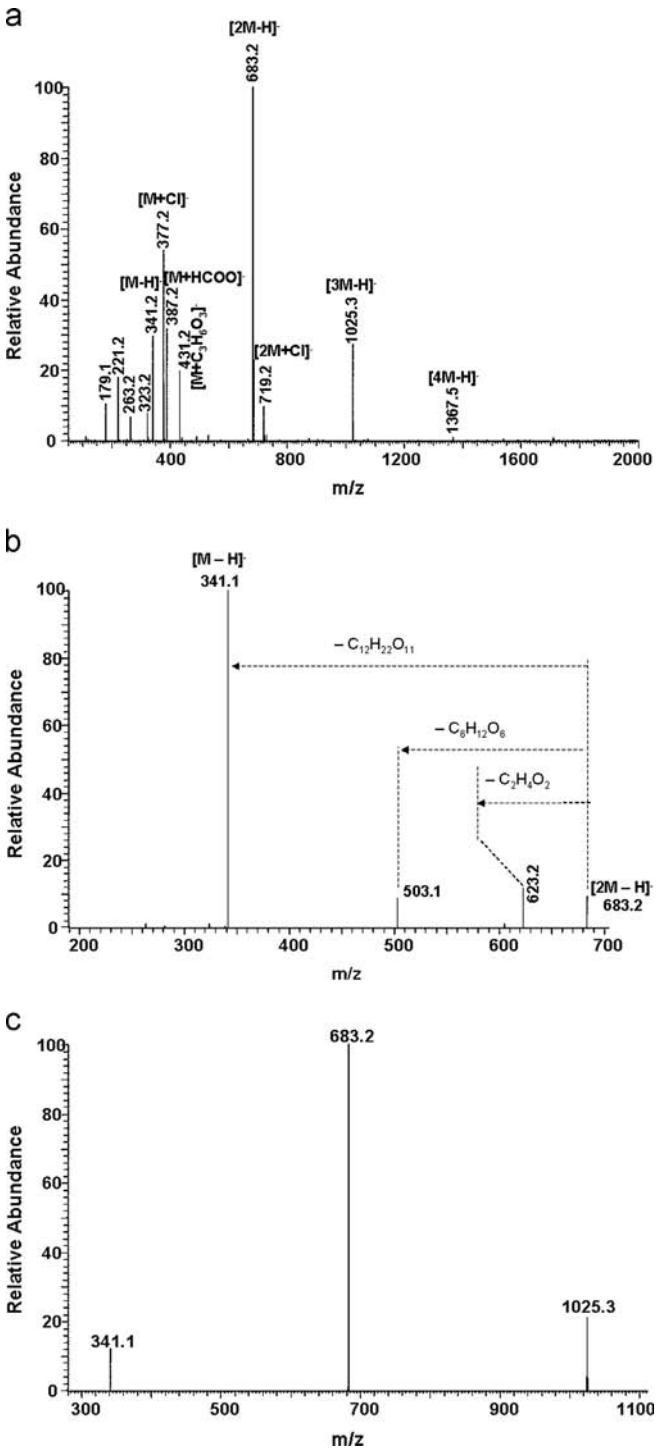

Fig. 1. (a) ESI full-scan mass spectrum of cellobiose in negative ion mode; negative tandem mass spectra of the dimer ion (b) and trimer ion (c) of cellobiose. Conditions were given in the Supporting information.

should be formed by the non-covalent interaction between the negative and neutral monomers.

The fragmentation of the dimer ion at *m/z* 683 yielded the major deprotonated ion $[M-H]^-$ at *m/z* 341 arising from the neutral loss of one disaccharide molecule and small amounts of ions at *m/z* 623 and 503, as illustrated in Fig. 1b. Based on the *m/z* value of the fragment ions at *m/z* 623 and 503, they were determined to be formed from the neutral losses of $C_2H_4O_2$ (-60 Da) and $C_6H_{10}O_5$ (-162 Da), respectively. Therefore, it was easy to deduce that these product ions must be formed directly from the dissociation of the dimer without the breakdown of the non-covalent complex. The fragmentation of the $[3M-H]^-$ at *m/z* 1025 is illustrated in Fig. 1c. Unlike the fragmentation of the dimer ion at *m/z* 683 that yielded fragment ions arising from both noncovalent and covalent bond dissociation simultaneously, the trimer generated product ions only from the noncovalent bond dissociation, yielding the ion at *m/z* 683 and the ion at *m/z* 341, which was formed from the loss of one and two disaccharide molecule, respectively. As for the dimers of the other disaccharide isomers, the same fragmentation patterns could also be observed.

3.2. Ionization mechanism of the deprotonated dimer ions

It is well-known that the intermolecular interaction energy (binding energy) is a quantitative indicator of the strength of interaction, and its magnitude could be used to measure the relative stability of a dimer [19]. To explain the phenomena reasonably, theoretical calculation was employed by the software package Gaussian 09, as described above. As previously reported, [6] the deprotonation of reducing carbohydrate occurred on the hemiacetal hydroxyl at the reducing end. By optimizing the experimental parameters, the equilibrium configuration of the non-covalent dimer of cellobiose is established, as depicted in Fig. 2. The interatomic distance between O1 and H is 1.07 Å, while the interatomic distance between O2 and H is 1.42 Å, both of which are longer than the normal covalent bond length of O–H (0.96 Å). It indicates that the two hemiacetal hydroxyl oxygens share one hydrogen atom, making the two monomers to get close to each other. Furthermore, the intermolecular interaction energy was calculated to be -330.65 kJ/mol, which was close to the bond energy of the C–C bond (347 kJ/mol) or the C–O bond (358 kJ/mol). That is the reason why some fragmentation of intramolecular sugar bonds had preceded the breakdown of the non-covalent complex.

Since the usual hydrogen bond energy is at the range of -21 to -29 kJ/mol, it is easy to deduce that the strong interaction force between the two adjacent monomers is mainly from the two hemiacetal hydroxyl oxygen atoms sharing one proton. The conclusion was further proved by the comparison with the negative full-scan mass spectrometric analysis of sucrose, a non-reducing disaccharide without hemiacetal hydroxyl. As depicted in Fig. 3a, the predominant peak is the deprotonated monomer ion at *m/z* 341, accompanied with minor dimer ion, whose relative abundance is lower than 20%. The reason is that the sucrose has no hemiacetal

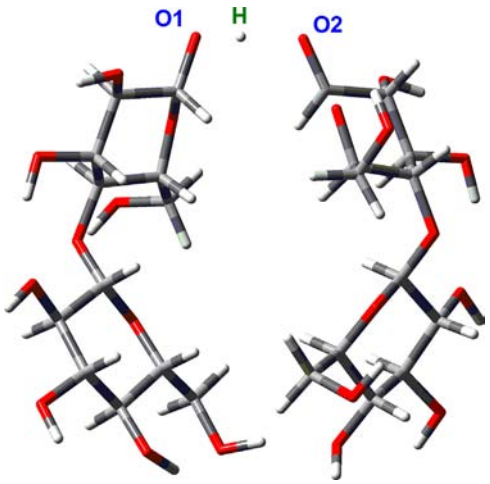

Fig. 2. Optimized computer modeling structure of deprotonated dimer of cellobiose.

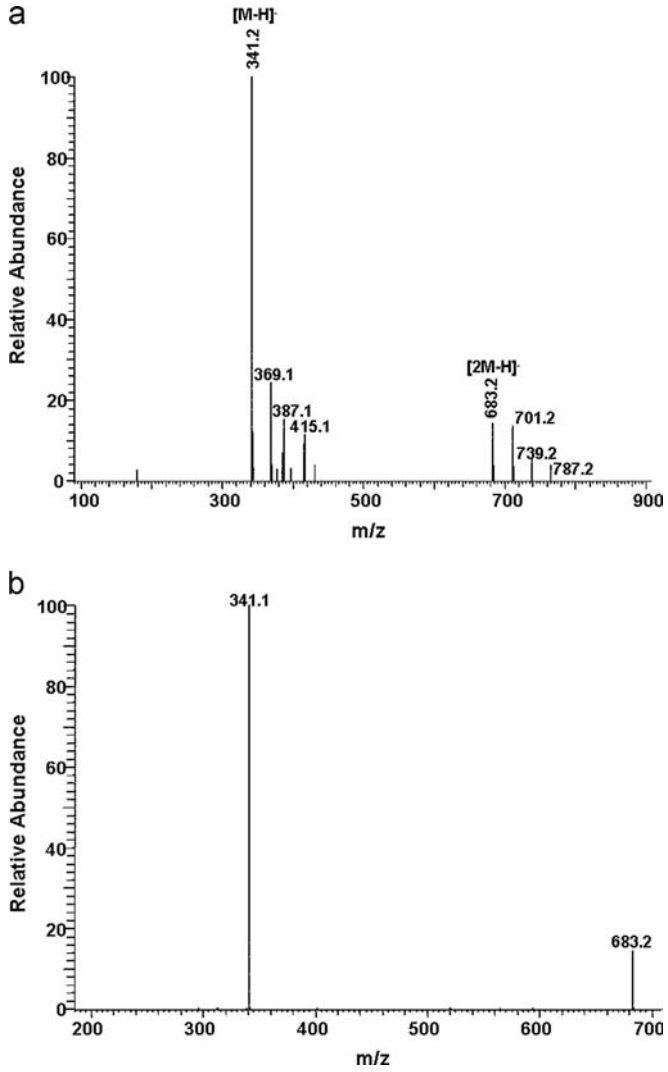

Fig. 3. (a) ESI full-scan mass spectrum of sucrose in negative ion mode and (b) negative tandem mass spectrum of the deprotonated dimer of sucrose. The CID energy, used to preserve a signal of the precursor ion in the range of 5–20%, was 7%.

hydroxyl, and the interaction force between the deprotonated ion and neutral molecule is only from the multiple hydrogen bonds. The tandem mass spectrum of the dimer of sucrose, depicted in Fig. 3b, shows only the fragment ion at *m/z* 341 derived from the dissociation of the common non-covalent bond. The CID energy, used to preserve a signal of the precursor ion in the range of 5–20%, was 7%, lower than that of reducing one. It further illustrated that the formation process for the reducing oligosaccharide dimers seemed as a chemical reaction forming a new bond, rather than the two monomers attracted each other and fell toward each other. It is consistent with the above conclusion of the tandem mass spectrometric analysis that the dimers are not the common non-covalent bonded ions. The further tandem mass spectrometric analysis of $[3M-H]^-$ (Fig. 1c) illustrated that the sharing proton structures had a certain saturation. As for the trimer, two of the three monomers still shared one proton forming dimer and the third monomer cohered loosely to the dimer only by intermolecular hydrogen bond.

3.3. Tandem mass spectrometric analysis of disaccharide dimers

The characterization of disaccharide isomers has always been a hot research spot [8,11,20–22]. In this study, extra diagnostic information can be gained from the investigation of the fragmentation pathways of $[2M-H]^-$ ions. The fragmentation of dimers could yield the product ions from the cleavage of covalent bond, providing us a new method to investigate the disaccharide isomers. Under the same measurement conditions, both the patterns and the relative ion abundances of fragment ions arising from disaccharide dimers depended on the disaccharide linkage types and anomeric configurations. Furthermore, fragmentations of the deprotonated disaccharide dimers were obviously different from that of chloride adducts of disaccharides, since the collision energy in the above experiment had been mainly dispersed for the dissociation of dimers into momers. By comparison of tandem mass spectra of chloride adducts of disaccharides, some product ions from the dissociation needing more collision energy have not be detected in that of deprotonated dimers, i. e. fragment ions formed from the loss of $C_2H_6O_3$ (−78 Da) in 1-2 linked disaccharides (Fig. 4a and b vs Fig. S-3a and S-3b); fragment ions formed from the loss of $C_3H_6O_3$ (−90 Da) of 1-3 linked disaccharides (Fig. 4c and d vs Fig. S-3c and S-3d); fragment ions formed from the loss of $C_2H_6O_3$ (−78 Da) and fragment ions from the loss of $C_4H_8O_4$ (−120 Da) in 1-4 linked disaccharides (Fig. 4e and f vs Fig. S-3e and S-3f); fragment ions formed from the loss of $C_4H_8O_4$ (−120 Da) in 1-6 linked disaccharides (Fig. 4g and h vs Fig. S-3g and S-3h). Therefore, it can be easy to identify the linkage disaccharides by the fragmentation of deprotonated dimers.

The CID-MS/MS spectra of α(1→2)-linked kojibiose and β(1→2)-linked sophorose illustrated in Fig. 4a and b, respectively. The major ions at *m/z* 341 correspond to the deprotonated monomer ion arising from the breakdown of non-covalent bond. The ions at *m/z* 665 and 647 are formed from the loss of one and two H_2O, respectively. The cross-ring cleavage ions at *m/z* 563 and the glycosidic cleavage ions at *m/z* 521 are formed from the neutral loss of $C_4H_8O_4$ and one glucose residue, respectively. Several fragment ions at *m/z* 323, 263 and 221 formed from further dissociation of deprotonated monomer ion (i. e. *m/z* 341) also can be observed. The anomeric configurations of kojibiose and sophorose can be easily assigned based on the relative abundance ratio of *m/z* 563:521, larger than 1 (α isomer in Fig. 4a) or smaller than 1 (β isomer in Fig. 4b).

Compared to the spectra of (1→2)-linked disaccharides, Fig. 4c and d clearly shows that the presence of the ion at *m/z* 503 arising from the loss of one glucose molecule ($C_{12}H_{22}O_{11}$, 180 Da), of which the high abundances are typical for the spectra of (1→3)-linked disaccharides. The biggest difference between the two anomers is the relative ion intensity of the peak at *m/z* 503 (higher in α(1→3)-linked one and smaller in β(1→3)-linked one). The (1→4)-linked disaccharides can be distinguished from the (1→2)-linked disaccharides by simply checking the appearance of fragment ions at *m/z* 623 and 503, which are formed from the neutral loss of $C_2H_4O_2$ (−60 Da) and $C_{12}H_{22}O_{11}$ (−180 Da), respectively. The clear-cut differentiation between the α- and β-configurations in the (1→4)-linked disaccharides is the relative ion intensity of the fragment ion at *m/z* 281 arising from further dissociation of deprotonated monomer ion (i. e. *m/z* 341) and the relative abundance ratio of *m/z* 503:623, which is larger than 1 in Fig. 4e (α isomer) and smaller than 1 in Fig. 4f (β isomer). As for the 1-6 linked disaccharides, the observation of fragment ions at *m/z* 623, 593 and 521 (Fig. 4g and h) is the characteristic of the α(1→6) glycosyl linkages. They are formed from the loss of $C_2H_4O_2$, $C_3H_6O_3$ and $C_6H_{10}O_5$, respectively. The fragment ions at *m/z* 323, 263 and 221 are assigned as dehydration ion, ^{0,2}A-ion and ^{0,4}A-ion, respectively, which are formed from further dissociation of deprotonated monomer ion. By comparison of α(1→6)-linked isomaltose and β(1→6)-linked gentiobiose, the appearance of fragment ions at *m/z* 623 and 593 but the absence of ion at *m/z* 521 is indicative of the β(1→6) glycosyl linkages.

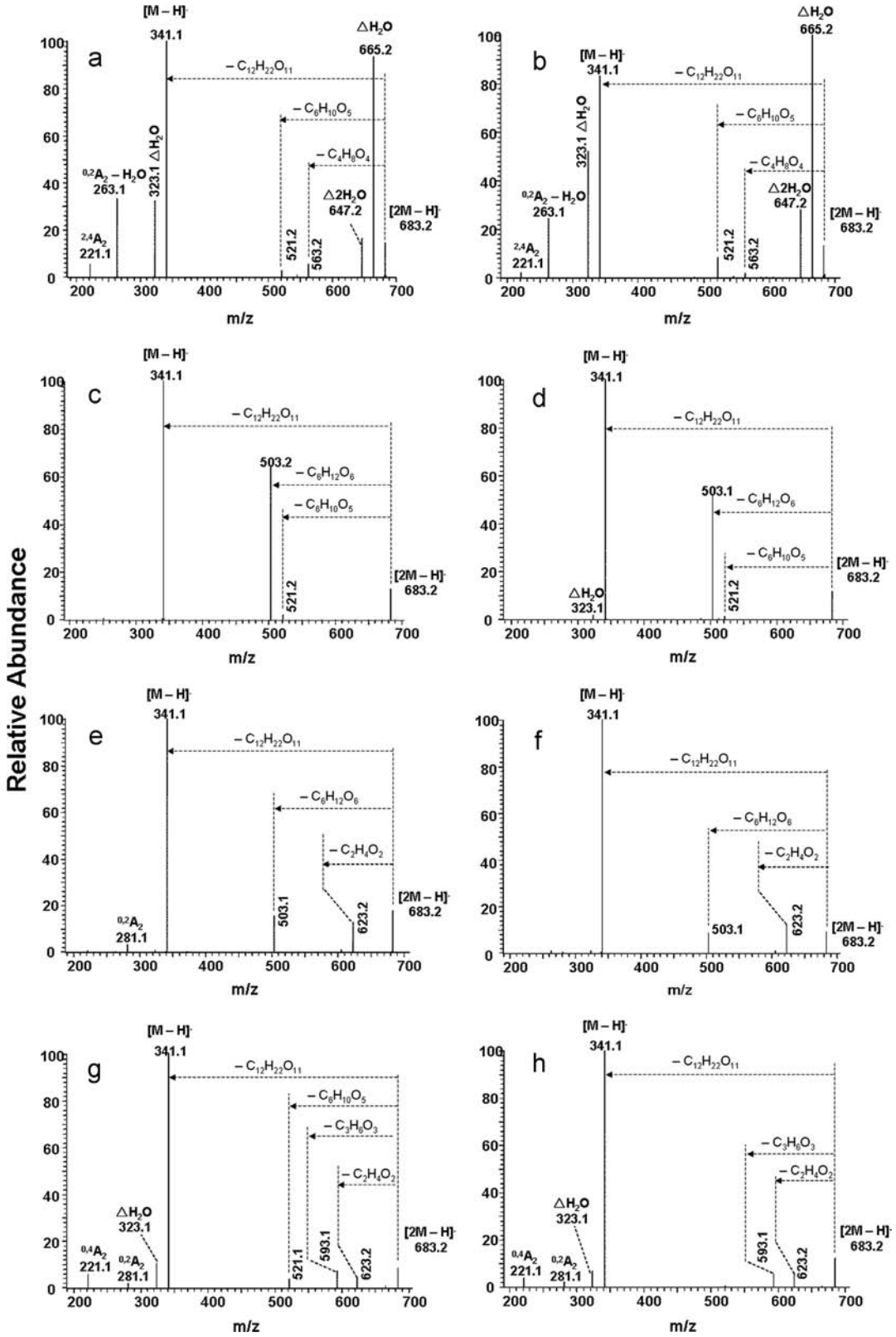

Fig. 4. Tandem mass spectra of deprotonated dimer ions of reducing disaccharide isomers. (a) kojibiose, (b) sophorose, (c) nigerose, (d) laminaribiose, (e) maltose, (f) cellobiose, (g) isomaltose and (h) gentiobiose. The Domon and Costello nomenclature [23] has been employed to define several fragment ions.

4. Conclusions

One novel highly stable and approximately symmetric disaccharide dimer was discovered in ESI-MS and several fragment ions arising from the dissociation of covalent bonds without destroying the non-covalent bonds were detected in ESI-MS/MS. Density functional theory (DFT) level using the B3LYP functional and the 6-31+G(d,p) basis set was employed to find the reason why it happened. The result showed that the two hemiacetal hydroxyl oxygen atoms shared one proton and the intermolecular

interaction energy was close to the bond energy of the C–C bond and the C–O bond. By investigating the fragmentation pathways of $[2M-H]^-$ ions, extra diagnostic information had been gained to distinguish the glucose-containing disaccharide isomers. This work improved our understanding of behavior of carbohydrate in the negative mass spectrometry, which would open the new view to investigate carbohydrate.

Acknowledgment

This work was supported by the National Natural Science Foundation of China (No. 21175127) and the Project supported by the National Science and Technology Ministry (ID: 2011 BAI03B01). And we also heartily thank Junling Jin from the Faculty of Chemistry of Northeast Normal University for providing the computational supports.

Appendix A. Supplementry material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.talanta.2013.06.055.

References

[1] J.F. Rakus, L.K. Mahal, New technologies for glycomic analysis: toward a systematic understanding of the glycome, Ann. Rev. Anal. Chem. *4* (2011) 367–392.
[2] K. Bock, J. Schuster-Kolbe, E. Altman, G. Allmaier, B. Stahl, R. Christian, U.B. Sleytr, P. Messner, Primary structure of the O-glycosidically linked glycan chain of the crystalline surface layer glycoprotein of thermoanaerobacter thermohydrosulfuricus L111-69. Galactosyl tyrosine as a novel linkage unit, J. Biol. Chem. 269 (1994) 7137–7144.
[3] U. Zaehringer, F. Wagner, E.T. Rietschel, G. Ben-Menachem, J. Deutsch, S. Rottem, Primary structure of a new phosphocholine-containing glycoglycerolipid of mycoplasma fermentans, J. Biol. Chem. *272* (1997) 3511–3519.
[4] D.J. Harvey, Analysis of carbohydrates and glycoconjugates by matrix-assisted laser desorption/ionization mass spectrometry: an update for the period 2005–2006, Mass Spectrom. Rev. 30 (2011) 1–100.
[5] A. Dell, H.R. Morris, Glycoprotein structure determination by mass spectrometry, Science 291 (2001) 2351–2356.
[6] J. Zaia, Mass spectrometry of oligosaccharides, Mass Spectrom. Rev. 23 (2004) 161–227.
[7] G.E. Hofmeister, Z. Zhou, J.A. Leary, Linkage position determination in lithium-cationized disaccharides: tandem mass spectrometry and semiempirical calculations, J. Am. Chem. Soc. 113 (1991) 5964–5970.
[8] J. Simoes, P. Domingues, A. Reis, F.M. Nunes, M.A. Coimbra, R.M. Domingues, Identification of anomeric configuration of underivatized reducing glucopyranosyl-glucose disaccharides by tandem mass spectrometry and multivariate analysis, Anal. Chem. 79 (2007) 5896–5905.
[9] B. Mulroney, J.C. Traeger, B.A. Stone, Determination of both linkage position and anomeric configuration in underivatized glucopyranosyl disaccharides by electrospray mass spectrometry, J. Mass Spectrom. 30 (1995) 1277–1283.
[10] W.G. Chai, V. Piskarev, A.M. Lawson, Negative ion electrospray mass spectrometry of neutral underivatized oligosaccharides, Anal. Chem. 73 (2001) 651–657.
[11] T.T. Fang, B. Bendiak, The stereochemical dependence of unimolecular dissociation of monosaccharide-glycolaldehyde anions in the gas phase: a basis for assignment of the stereochemistry and anomeric configuration of monosaccharides in oligosaccharides by mass spectrometry via a key discriminatory product ion of disaccharide fragmentation, *m/z* 221, J. Am. Chem. Soc. 129 (2007) 9721–9736.
[12] R. Cmelik, M. Stikarovska, J. Chmelik, Different behavior of dextrans in positive-ion and negative-ion mass spectrometry, J. Mass Spectrom. 39 (2004) 1467–1473.
[13] R. Cmelik, J. Chmelik, Structural analysis and differentiation of reducing and nonreducing neutral model starch oligosaccharides by negative-ion electrospray ionization ion-trap mass spectrometry, Int. J. Mass Spectrom. 291 (2010) 33–40.
[14] Y. Jiang, R.B. Cole, Oligosaccharide analysis using anion attachment in negative mode electrospray mass spectrometry, J. Am. Soc. Mass Spectrom. 16 (2005) 60–70.
[15] L. Boutegrabet, B. Kanawati, I. Gebefuegi, D. Peyron, P. Cayot, R. Gougeon, P. Schmitt-Kopplin, Attachment of chloride anion to sugars: mechanistic investigation and discovery of a new dopant for efficient sugar ionization/detection in mass spectrometers, Chem.-Eur. J. 18 (2012) 13059–13067.
[16] C.E.V. Seggern, R.J. Cotter, Fragmentation studies of noncovalent sugar–sugar complexes by infrared atmospheric pressure MALDI, J. Am. Soc. Mass Spectrom. 14 (2003) 1158–1165.
[17] A.D. Becke, Density-functional thermochemistry. III. The role of exact exchange, J. Chem. Phys. 98 (1993) 5648–5652.
[18] C.E. Von Seggern, S.C. Moyer, R.J. Cotter, Liquid infrared atmospheric pressure MALDI/ion trap mass spectrometry of sialylated carbohydrates, Anal. Chem. 75 (2003) 3212–3218.
[19] J. Vura-Weis, M.A. Ratner, M.R. Wasielewski, Geometry and electronic coupling in perylenediimide stacks: mapping structure-charge transport relationships, J. Am. Chem. Soc. 132 (2010) 1738–1739.
[20] M.R. Schenauer, J.K. Meissen, Y. Seo, J.B. Ames, J.A. Leary, Heparan sulfate separation, sequencing, and isomeric differentiation: ion mobility spectrometry reveals specific iduronic and glucuronic acid-containing hexasaccharides, Anal. Chem. 81 (2009) 10179–10185.
[21] S.E. Stefan, M. Ehsan, W.L. Pearson, A. Aksenov, V. Boginski, B. Bendiak, J.R. Eyler, Differentiation of closely related isomers: application of data mining techniques in conjunction with variable wavelength infrared multiple photon dissociation mass spectrometry for identification of glucose-containing disaccharide ions, Anal. Chem. 83 (2011) 8468–8476.
[22] M. Major, T. Fouquet, L. Charles, Isomeric distinction of small oligosaccharides: a bottom-up approach using the kinetic method, J. Am. Soc. Mass Spectrom. 22 (2011) 1252–1259.
[23] B. Domon, C.E. Costello., A systematic nomenclature for carbohydrate fragmentations in FAB-MS/MS spectra of glycoconjugates, Glycoconjugate J. 5 (1988) 397–409.