磁搅拌条件下 β -环糊精与亚砷酸钠加合物的形成、 谱学特性与热分解行为

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摘要: 傅里叶变换利用红外光谱、粉末 X 射线衍射、微分热重分析、气相色谱-飞行时间质谱、紫外光谱、 ^1H 核磁滴定以及电喷雾质谱等分析手段对 β -环糊精(β -CD)和亚砷酸钠(SA)形成的分子-离子加合物 SA- β -CD 进行了详细表征. 结果显示, 主-客体之间分子-离子相互作用是导致 SA- β -CD 的谱学特性(在固态或在溶液中)与热分解行为相异于主、客体自身行为的重要原因. 而在气相色谱-飞行时间质谱条件下发生的氧化还原反应以及在电喷雾质谱条件下出现的 Na^+ - β -CD(摩尔比为1:1)超分子离子复合体进一步揭示了这种分子-离子加合作用的复杂性与独特性.

关键词: β -环糊精; 亚砷酸钠; 加合物; 分子-离子相互作用; 无机药物

中图分类号: O643; O642

Preparation, Spectral Properties and Decomposition Behavior of a Novel β -Cyclodextrin and Sodium Arsenite Adduct Formed by Stirring

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Abstract: We report on the formation of a molecule-ion adduct of β -cyclodextrin (β -CD) with sodium arsenite (SA) both in solid state and in aqueous solution. The adduct was characterized using Fourier transform infrared spectroscopy, powder X-ray diffraction, differential thermogravimetric analysis, gas chromatography coupled to time-of-flight mass spectrometry, UV-Vis spectroscopy, ^1H nuclear magnetic resonance titration and electrospray ionization mass spectrometry. We found that a weak molecule-ion interaction was responsible for the difference in spectral properties in solid state and in aqueous solution as well as for the difference in thermal decomposition behavior between β -CD, SA and the adduct. The novelty and complexity of this interesting molecule-ion interaction was revealed by a redox reaction based on the data of gas chromatograph coupled to time-of-flight mass spectrometer and by the formation of the 1:1 (molar ratio) supramolecular ion complex, Na^+ - β -CD, based on its electrospray ionization mass spectrum.

Key Words: β -Cyclodextrin; Sodium arsenite; Adduct; Molecule-ion interaction; Inorganic drug

β -Cyclodextrin (β -CD) is a cyclic oligosaccharide consisting of seven glucose subunits connected through glycosidic α -1,4 bond, possessing a structure like a hollow truncate form with one ring wider than the other (Fig.1)^[1-3]. β -CD can form inclusion complexes with many kinds of guests such as organic molecules, polymers and coordination compounds^[4-6]. In many years, most studies are confined to systems involved in molecule-molecule

interactions between β -CD and organic drugs^[7,8]. Less attention has been paid to the formation, spectral characterization and thermal behavior of molecule-ion adducts between β -CD and classic inorganic drugs, though inorganic ions usually exist in host-guest systems as a buffer solution^[9].

According to this, sodium arsenite (NaAsO_2 , SA, see Fig.1), an important anticancer drug^[10], is chosen as the guest in this work,

Received: January 6, 2009; Revised: February 18, 2009; Published on Web: March 23, 2009.

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安徽省自然科学基金资助项目

Fig.1 Structural feature of β -CD and NaAsO_2

with the object of evaluating whether there is a molecule-ion interaction between SA and β -CD, and if yes, how it is related to the spectral property of β -CD both in solid state and in aqueous solution as well as to the thermal decomposition behavior of β -CD.

We believe that the present study on the construction, characterization and decomposition of the novel adduct, SA- β -CD, based on the molecule-ion interaction between host and guest, is important and significant not only in the field of supramolecular chemistry, but also in many other fields. For example, β -CD is widely applied to modulate the size and shape of nanoparticles in the crystal growth of inorganic salts^[11-13]. However, the molecule-ion interactions between them have not been described in detail yet. Hence, our results in this work may be expected to attract more attention to the study on molecule-ion interactions.

1 Experimental

1.1 Materials

β -CD was purchased from Shanghai Chemical Reagent Company ($\geq 98.0\%$) and recrystallized twice from deionized water. SA was purchased from Sigma (98.0%) and used without further purification.

1.2 Preparation of the physical mixture 1 and adduct 2 of β -CD with SA

The physical mixture **1** of β -CD with SA was prepared by mixing SA to β -CD in powder state with the molar ratio of 1:1. The adduct **2** of β -CD with SA was prepared by mixing β -CD with SA in molar ratio of 1:1 in aqueous solution, and stirred fiercely at 333 K for 4 h. Then the solution was dried into a powdery starting material in vacuo, and kept in a desiccator. The dried adduct powder is light yellow, while both β -CD and the mixture are pure white.

1.3 Instrument and method

Fourier transform infrared (FT-IR) spectra of several samples were recorded on a Bruker EQUINOX55 spectrometer in KBr pellets of the injected samples in the range of 4000–400 cm^{-1} . Powder X-ray diffraction (PXRD) measurements were performed on a Philips X'Pert Pro X-ray diffractometer. The samples were irradiated with monochromatized $\text{Cu } K_\alpha$ and analyzed with $5^\circ \leq 2\theta \leq 40^\circ$. The voltage and current were 40 kV and 40 mA, respectively. Differential thermogravimetric (DTG) curves were ob-

tained on a Shimadzu TGA-50 thermogravimetric analyzer at a heating rate of 10 $\text{K} \cdot \text{min}^{-1}$ under a nitrogen gas flow of 25 $\text{mL} \cdot \text{min}^{-1}$. The mass of crystallite powders is about 10.0 mg for the various DTG measurements. Gas chromatography coupled to time-of-flight mass spectrometry (GC-TOF-MS) was carried out using a Micromass GCT-MS spectrometer by means of the standard direct insertion probe for solid samples, with an increasing temperature. Experimental conditions were summarized as follows. At first, samples were kept at 303 K for 3 min, and then heated to 363 K at a heating rate of 80 $\text{K} \cdot \text{min}^{-1}$, and kept for 5 min. With the same heating rate, the temperature of samples was increased to 463 K. Subsequently, the samples were kept for 6 min in 463 K, further heated to 553 K. After kept for 7 min, the samples were continuously heated to 653 K at the heating rate of 80 $\text{K} \cdot \text{min}^{-1}$ and kept for 5 min. Finally, the samples were heated to 773 K at a heating rate of 100 $\text{K} \cdot \text{min}^{-1}$ and kept for 3 min^[14].

Electrospray ionization mass spectrum (ESI-MS) was recorded on Finnigan MS LCQ electrospray ionization mass spectrometer using 1:1 acetonitrile/deionized water as solvent. Injector pump was used for the sample.

UV-Vis absorption spectra were recorded on a Shimadzu UV 2401-(PC) UV/Vis spectrophotometer using quartz cells of 1.0 cm path at room temperature. In UV-Vis spectroscopy measurements, the stock solutions of β -CD and SA were prepared by dissolving solid samples in deionized water. The aqueous solutions to be detected were freshly prepared by diluting the stock solutions with deionized water. The concentration of SA in sample solutions is kept constant at $5.0 \times 10^{-4} \text{ mol} \cdot \text{L}^{-1}$, and the concentration of β -CD varied from 0 to $4.0 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$. ^1H NMR spectra were performed on a Bruker NMR spectrometer operating at 300 MHz by addition of SA to a series of β -CD solutions at 298 K. The chemical shifts of proton signals in β -CD were recorded with β -CD concentration kept constant ($1.0 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$), while the concentration of SA was gradually increased from 0 to $2.0 \times 10^{-2} \text{ mol} \cdot \text{L}^{-1}$.

2 Results and discussion

2.1 Comparison of FTIR spectra of β -CD, SA, physical mixture 1 and adduct 2

As could be seen from Fig.2, the absorption bands appearing

Fig.2 FT-IR spectra of (a) SA, (b) β -CD, (c) physical mixture 1, and (d) adduct 2

at about 1157, 1080, and 1029 cm^{-1} in the FT-IR curves of free β -CD, **1**, and **2** corresponded to the stretch vibrations of C—O and C—O—C of glucose units, and the bands at about 2900 and 3400 cm^{-1} were ascribed to the symmetric stretching vibration of CH_2 groups and the stretching vibration of OH groups of glucose units, respectively^[15].

After adducted, the stretching vibration band of OH groups tended to a slight red shift, from 3414 to 3398 cm^{-1} , indicating that hydrogen bonding interactions between β -CD molecules were enhanced in the presence of SA^[14]. Further, there was no occurrence of the patterns of SA in the physical mixture or the obtained adduct, which should be attributed to the low mass ratio of SA to β -CD in the two samples.

2.2 Comparison of PXRD curves of β -CD, SA, **1** and **2**

The PXRD spectra of β -CD, SA, **1** and **2** were illustrated in Fig.3. β -CD had three main peaks at 2θ values of 12.6°, 19.3° and 9.1°, indicating the existence of a cage-form structure^[16]. And the PXRD spectrum of **1** was the superposition of spectra of β -CD and SA. There was no large change in the stacking form of β -CD molecules in the formation of the adduct **2**, since almost all the main peaks of β -CD were displayed in the spectrum of **2**. However, those major peaks due to β -CD at lower 2θ angles shifted to high angles slightly. For instance, the first strongest peak at 12.6° in β -CD had shifted to 12.7° in **2**, suggesting closer distances between β -CD molecules upon adduct. Besides, the second strongest peak at 19.3° of β -CD became a double peak in **2**.

It also could be seen that the main peaks of SA, which had a crystal packing of primitive orthorhombic, almost completely disappeared in the spectrum of **2**. This phenomenon meant that the adduct was not a normal mixture but experienced an inelastic scatter process of SA through inserting into the molecular arrangement of β -CD in different directions, revealing that the stacking form of **2** was dominated by of β -CD^[17].

2.3 Comparison of DTG profiles of β -CD, **1** and **2**

The DTG curves of β -CD, **1** and **2** were depicted in Fig.4. The weak peaks at about 353 to 373 K in the three curves were ascribed to the release of water molecules^[17]. Clearly, in the appearance of SA, the release process of water was relatively gen-

Fig.3 PXRD spectra of (a) SA, (b) β -CD, (c) physical mixture **1**, and (d) adduct **2**

Fig.4 Ratio of fractional mass loss per second (v) to temperature

tle, and possessed a higher release temperature of about 20 K. This meant that water molecules existed in different forms in the absence and presence of SA. In addition, the strong peaks at about 593 K were attributed to the melting-decomposition of β -CD^[18,19]. While pure β -CD showed an acute evanescent decomposition behavior, such processes of the other two samples were provided with a longer and gentler curvature. As shown in Fig.4, the decomposition temperature points of the three samples had an approximately 10 K higher temperature from β -CD to **1** to **2**.

2.4 Analyses of GC-TOF-MS data of β -CD and **2**

In as much as there existed quite different decomposition behaviors of β -CD before and after adduct, these observations prompted us to evaluate in detail the difference between the decomposition processes of β -CD and the adduct **2** by means of GC-TOF-MS data.

The main peaks in the total ion current (TIC) curves of β -CD and **2** were listed in Table 1^[20], including heating time (t , min) and relative abundances (RA, %) of these peaks. There were only two main peaks (at 25.64 and 27.19 min) in the TIC curve of pure β -CD, with a small time interval (Δt , 1.55 min) and high intensities^[14]. However, for the adduct **2**, there were four main peaks in the TIC, each having completely different characteristics in terms of temperature (T), t and RA^[20].

According to Table 1, at low temperature (<653 K), pure β -CD has not undergone a mass loss larger than 5% of RA, but **2** released some of its mass at 17.52 min, i.e., at about 553 K. It meant that in the presence of SA, some of β -CD molecules had a lower decomposition temperature. Maybe some of the covalent bonds in those released β -CD molecules were weakened by the molecule-ion interaction between β -CD and SA.

Fig.5 showed the mass spectra at 17.33 min of the two sam-

Table 1 Main peaks in the TIC curves of β -CD and **2**^[20]

Compound	t /min	T /K	RA(%)
β -CD	25.64	653	100.00
	27.19	653	70.16
2	17.52	553	24.57
	25.13	633	100.00
	31.52	733	20.33
	35.74	733	9.68

Fig.5 Mass spectrum of adduct **2** at 17.33 min and 553 K

The inset is the mass spectrum of free β -CD at 553 K.

ples. It was clear that the fragment at m/z 44 (CO_2^+) had the highest relative abundance of 100% in the two spectra, and there were no other strong fragment peaks appearing in the spectrum of **2**, which was considerably different from that of pure β -CD. In the light of DTG profiles, TIC data and Fig.5, the structure of β -CD was not completely destroyed at 553 K.

Fig.6 showed the mass spectrum of **2** at 25.13 min and 633 K. From TIC data, it could be found that β -CD (at the top of peak) and **2** (still at the foot of peak)^[20] would be experiencing a fierce decomposition process at the moment. Indeed, the results of Fig. 6 and its inset revealed that the decomposition modes of them were rather different. Unlike pure β -CD, most of the major fragments larger than 20% of RA in the spectrum of **2**, such as OH^+ , H_2O^+ , CH_3O^+ , CO_2^+ , were quite small, implying that the intermolecular interactions between β -CD molecules had changed drastically in the influence of SA. However, several key fragments referring to the covalent bonds at the same glucose groups in the spectrum of β -CD also appeared in that of **2**, such as 60 ($\text{C}_2\text{H}_4\text{O}_2^+$), 73 ($\text{C}_3\text{H}_5\text{O}_2^+$)^[14], indicating that a few β -CD molecules in the adduct **2** were in different circumstances from the other, because they did not change and were kept the same as the decomposition behavior of β -CD.

It was interesting that only for just an instant later (Fig.7), the decomposition mode of the adduct **2** was altered dramatically,

Fig.6 Mass spectrum of adduct **2** at 25.13 min and 633 K

The inset is the mass spectrum of free β -CD at 633 K.

Fig.7 Mass spectrum of adduct **2** at 25.53 min and 633 K

while there was no difference in that of β -CD. In Fig.7, four new fragments with fine proportionate relationships related to m/z values appeared. The four fragment peaks at m/z of 75, 150, 225, and 300 were As^+ (RA, 3.27%), As_2^+ (4.85%), As_3^+ (1.97%), and As_4^+ (24.95%), respectively^[20,21]. And their stabilities decreased in the order of $\text{As}_4^+ > \text{As}_3^+ > \text{As}_2^+ > \text{As}^+$. The liberation behavior of arsenic possibly suggested that a redox reaction had occurred in the inducement of the carbonized β -CD.

2.5 Analyses of UV-Vis spectra of SA in the presence of β -CD

The weak molecule-ion interaction between β -CD and SA had been proved in solid state. But we know that, all oral drugs should be dissolved before they were assimilated by human organism^[22]. Whether is the weak interaction presented in aqueous solution like in solid state?

In aqueous solution, SA would be converted totally into AsO_2^- ions. As shown in Fig.8, the absorption intensity of the AsO_2^- ions at the maximum absorbance wavelength of 204 nm gradually increased with increasing the concentration of β -CD, indicating that there was a change of chemical circumstances around the AsO_2^- ions. This finding can be attributed to the ionic transference of the AsO_2^- ions from a highly polar environment of an aqueous solution to the cavity rims of β -CD molecules through intermolecular interaction between the hydrogen atoms of the

Fig.8 UV-Vis spectra of SA ($5.0 \times 10^{-4} \text{ mol} \cdot \text{L}^{-1}$) in the absence and presence of β -CD

The concentration of β -CD from a to i is 0.0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, and 4.0 $\text{mmol} \cdot \text{L}^{-1}$, respectively.

hydroxyl groups of β -CD and the anions.

It was worthy to note that β -CD itself had no absorption in the wavelength range from 195 to 210 nm, and there were no changes of pH and ionic strength before and after adduct.

2.6 Analyses of ^1H NMR spectra of β -CD in the presence of SA

^1H NMR titration could provide the structural information about the formed complexes or adducts according to observed chemical shift changes ($\Delta\delta$) of different proton signals of β -CD^[23,24]. Typical ^1H NMR spectra of β -CD at each titration point with or without SA were expressed in Fig.9. Apparently, the continuous chemical shift changes of the protons occurred with an increase in the molar ratio (R) of SA to β -CD.

As shown in Fig.9, a progressive increase of the $\Delta\delta$ values of the H-5 and H-6 protons of β -CD with increasing the relative concentration of SA was clearly observed. The maximum $\Delta\delta$ values of H-1, H-3, H-5, and H-6 protons were 0.0269, 0.0320, 0.0415, and 0.0415, respectively. The rather small $\Delta\delta$ values of the proton signals implied that the binding affinity of hydroxyl groups of β -CD, as well as its cavity, to SA was weak, which was in accordance with the reported results^[25,26] on the systems between CDs and other inorganic salts. Therefore, ^1H NMR titrations allowed us to make an estimate that in aqueous solution there was a weak molecule-ion interaction between AsO_3^- ions and β -CD.

2.7 Direct evidence of molecule-ion interactions from ESI-MS spectrum

ESI-MS technique is a useful method to investigate the formation and composition of CD inclusion complexes^[27,28]. The ESI-MS data of the adduct **2** (Fig.10) showed a principal peak at m/z 1157.56 (100%) and a minor molecular peak at m/z 1135.22 (28%), corresponding to the 1:1 supramolecular cation $[\text{Na-}\beta\text{-CD}]^+$ and $[\beta\text{-CD}]^+$ itself, respectively. These data provided a direct evidence that a molecule-ion interaction occurred between β -CD and a univalent cation Na^+ , which is quite different from our earlier work, for CDs are more likely to have interactions with anions such as NO_3^- ^[3].

Further, there are also some peaks revealing the formation of supramolecular cations such as the peak at m/z 587.22 (RA,

Fig.9 Chemical shifts (δ) of the proton signals of β -CD in the absence and presence of SA

R represents the molar ratio of SA to β -CD.

Fig.10 Electrospray ionization mass spectrum of system of SA with β -CD

41%), responding to $[\text{Na-}\beta\text{-CD}\cdot\text{H}_2\text{O}]^{2+}$.

3 Conclusions

Although the spectral changes in the molecule-ion system could be not comparable with those of molecule-molecule inclusion systems between β -CD and organic guests, it was important and significant for the demonstration of the existence of molecule-ion interactions because either inorganic salts as a third component (buffer solutions) usually existed in guest-CD inclusion systems or β -CD as an additive appeared in nanoparticle growth systems of inorganic salts. The molecule-ion interaction between β -CD and SA produced a certain effect on the thermal behavior of β -CD. A novel oxidation-reduction reaction was expected to occur between carbonized β -CD and SA along with the liberation of four kinds of simple substances of the element arsenic. Further, the molecule-ion interaction between SA and β -CD was observed in solution. And some direct evidences from ESI-MS experiments were presented to demonstrate the formation of molecule-ion adducts such as $[\text{Na-}\beta\text{-CD}]^+$. The study presented here offers some enlightenment to the issue related to the application of inorganic salts in cyclodextrin chemistry.

Acknowledgments: We would like to express our sincere thanks to Hao Yin in Structure Research Laboratory of Chinese Academy of Sciences for useful advice in the GC-TOF-MS measurements and to Gao Wu in Research Centre for Life Sciences, University of Science and Technology of China for useful discussion in the ESI-MS experiments.

References

- 1 Tong, L. H.; Shen, B. J. Physical methods in supramolecular chemistry study. Beijing: Science Press, 2004: 1–4 [童林荟, 申宝剑. 超分子化学研究中的物理方法. 北京: 科学出版社, 2004: 1–4]
- 2 Yang, Z. X.; Chen, Y.; Liu, Y. *Carbohydr. Res.*, **2008**, **343**: 2439
- 3 Song, L. X.; Teng, C. F.; Yang, Y. J. *Incl. Phenom. Macrocycl. Chem.*, **2006**, **54**: 221
- 4 Braga, S. S.; Gago, S.; Seixas, J. D.; Valente, A. A.; Pillinger, M.; Santos, T. M.; Goncalves, I. S.; Romao, C. C. *Inorg. Chim. Acta*,

- 2006, **359**: 4757
- 5 Lysik, M. A.; Wu, P. S. *J. Pharm. Sci.*, **2003**, **92**: 1559
- 6 Topchieva, I. N.; Tonelli, A. E.; Panova, I. G.; Matuchina, E. V.; Kalashnikov, F. A.; Gerasimov, V. I.; Rusa, C. C.; Rusa, M.; Hunt, M. A. *Langmuir*, **2004**, **20**: 9036
- 7 Zha, F.; Li, S. G.; Chang, Y. *Carbohydr. Polym.*, **2008**, **72**: 456
- 8 Marques, J.; Anjo, L.; Marques, M. P. M.; Santos, T. M.; Paz, F. A. A.; Braga, S. S. *J. Organomet. Chem.*, **2008**, **693**: 3021
- 9 Berto, S.; Bruzzoniti, M. C.; Cavalli, R.; Perrachon, D.; Prenesti, E.; Sarzanini, C.; Trotta, F.; Tumiatti, W. *J. Incl. Phenom. Macrocycl. Chem.*, **2007**, **57**: 631
- 10 Niu, C.; Yan, H.; Yu, T.; Sun, H. P.; Liu, J. X.; Li, X. S.; Wu, W.; Zhang, F. Q.; Chen, Y.; Zhou, L.; Li, J. M.; Zeng, X. Y.; Ouyang, R. R.; Yuan, M. M.; Ren, M. Y.; Gu, F. Y.; Cao, Q. B.; Gu, W.; Su, X. Y.; Chen, G. Q.; Xiong, S. M.; Zhang, T. D.; Waxman, S.; Wang, Z. Y.; Chen, Z.; Hu, J.; Shen, Z. X.; Chen, S. J. *Blood*, **1999**, **94**: 3315
- 11 Zhang, X. Y.; Liao, Z. J.; Yang, L.; Hu, Z. G.; Jiang, K.; Guo, Y. M. *Acta Chim. Sin.*, **2003**, **61**: 69 [张秀英, 廖照江, 杨林, 胡志国, 蒋凯, 郭玉明. 化学学报, **2003**, **61**: 69]
- 12 Zhao, B.; Chen, H. L. *Mater. Lett.*, **2007**, **61**: 4890
- 13 Lipowsky, P.; Jia, S.; Hoffmann, R. C.; Jin-Phillipp, N. Y.; Bill, J.; Ruhle, M. *Int. J. Mater. Res.*, **2006**, **97**: 607
- 14 Song, L. X.; Xu, P. *J. Phys. Chem. A*, **2008**, **112**: 11341
- 15 Song, L. X.; Wang, H. M.; Guo, X. Q.; Bai, L. *J. Org. Chem.*, **2008**, **73**: 8305
- 16 Magyar, A.; Szendi, Z.; Kiss, J. T.; Linko, I. P. *J. Mol. Struct. - Theochem*, **2003**, **666**: 163
- 17 Veiga, M. D.; Merino, M. *J. Pharm. Biomed. Anal.*, **2002**, **28**: 973
- 18 Saenger, W. *Angew. Chem., Int. Ed. Engl.*, **1980**, **19**: 344
- 19 Xu, P.; Song, L. X. *Acta Phys. -Chim. Sin.*, **2008**, **24**: 729 [徐鹏, 宋乐新. 物理化学学报, **2008**, **24**: 729]
- 20 Song, L. X.; Dang, Z. *J. Phys. Chem. B*, **2009**, **113**: 4998
- 21 Lynch, D. C. *Metal. Trans. B*, **1980**, **11**: 623
- 22 Dunne, A.; Devane, J.; O'Hara, T. *J. Roy. Stat. Soc. D-the Statistician*, **1999**, **48**: 125
- 23 Cao, Y. J.; Xiao, X. H.; Ji, S. F.; Lu, R. H.; Guo, Q. X. *Spectrochim. Acta A*, **2004**, **60**: 815
- 24 Song, L. X.; Wang, H. M.; Xu, P.; Zhang, Z. Q.; Liu, Q. Q. *Bull. Chem. Soc. Jpn.*, **2007**, **80**: 2313
- 25 Matsui, Y.; Ono, M.; Tokunaga, S. *Bull. Chem. Soc. Jpn.*, **1997**, **70**: 535
- 26 Song, L. X.; Bai, L.; Xu, X. M.; He, J.; Pan, S. Z. *Coord. Chem. Rev.*, **2009**, **253**: 1276
- 27 Cescutti, P.; Garozzo, D.; Rizzo, R. *Carbohydr. Res.*, **1996**, **290**: 105
- 28 Gabelica, V.; Galic, N.; de Pauw, E. *J. Am. Soc. Mass Spectr.*, **2002**, **13**: 946