J. Am. Soc. Mass Spectrom. (2017) 28:224–228
DOI: 10.1007/s13361-016-1519-5

RESEARCH ARTICLE

Enantiomeric Excess Determination for Monosaccharides Using Chiral Transmission to Cold Gas-Phase Tryptophan in Ultraviolet Photodissociation

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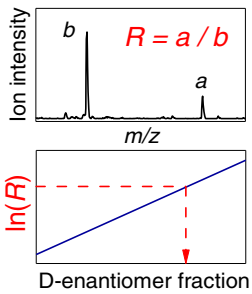

Abstract. Chiral transmission between monosaccharides and amino acids via photodissociation in the gas phase was examined using a tandem mass spectrometer fitted with an electrospray ionization source and a cold ion trap in order to investigate the origin of the homochirality of biomolecules in molecular clouds. Ultraviolet photodissociation mass spectra of cold gas-phase noncovalent complexes of the monosaccharide enantiomers glucose (Glc) and galactose (Gal) with protonated L-tryptophan H^+(L-Trp) were obtained by photoexcitation of the indole ring of L-Trp. L-Trp dissociated via C_α–C_β bond cleavage when noncovalently complexed with D-Glc; however, no dissociation of L-Trp occurred in the homochiral H^+(L-Trp)(L-Glc) noncovalent complex, where the energy absorbed by L-Trp was released through the evaporation of L-Glc. This enantioselective photodissociation of Trp was due to the transmission of chirality from Glc to Trp via photodissociation in the gas-phase noncovalent complexes, and was applied to the quantitative chiral analysis of monosaccharides. The enantiomeric excess of monosaccharides in solution could be determined by measuring the relative abundance of the two product ions in a single photodissociation mass spectrum of the cold gas-phase noncovalent complex with H^+(L-Trp), and by referring to the linear relationships derived in this work.

Keywords: Gas-phase cluster, Noncovalent complex, Molecular cloud, Chiral recognition, Enantioselective, Optical purity, Homochirality

Received: 5 August 2016/Revised: 27 September 2016/Accepted: 1 October 2016/Published Online: 13 October 2016

Introduction

Biomolecules can recognize chiral molecules. For instance, one enantiomer of a chiral drug may be highly toxic, while the other is medically effective. Thus, optical purity determination of chiral molecules is crucial in pharmaceutical science and industry. Analytical methods such as high-performance liquid chromatography, gas chromatography, capillary electrophoresis, and nuclear magnetic resonance (NMR) spectroscopy are currently used to determine the optical purity of chiral molecules [1, 2]. A number of chiral selectors and reagents have been developed in analytical science, and chiral recognition phenomena have been investigated extensively using NMR, X-ray crystallography, laser spectroscopy, and molecular orbital calculations [3–7]. Several analytical methods for chiral recognition using mass spectrometry-based techniques have been proposed over the past two decades because mass spectrometry is highly sensitive and suitable for analyzing mixtures [6–15]. Furthermore, NMR detection for mass-selected gas-phase ions by magnetic resonance acceleration techniques has been reported [16, 17].

Chiral recognition phenomena in living systems are attributed to homochirality in biomolecules, which consist of L-amino acids and D-sugars. The origin of homochirality is one of the most interesting phenomena in science. A hypothesis for the extraterrestrial origin of biomolecules has been proposed on the basis of several experimental and analytical studies, in which the abiotic formation of racemic amino acids occurs in interstellar molecular clouds, followed by the enantioselective photodestruction of the D-enantiomer with circularly polarized light [18–20]. This hypothesis for the extraterrestrial origin of enantiomeric enrichment has been supported by the excess L-amino acids found in the Murchison meteorite [18] and the discovery of the interstellar chiral molecule propylene oxide [21]. The chiral behavior of gas-phase serine clusters has been investigated using mass spectrometry [22]. Serine forms magic-number ionic clusters composed of eight serine units.

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The serine octamer clusters are very stable and exhibit a remarkable preference for homochirality.

Chemical processes in interstellar molecular clouds occur at low temperatures (10–100 K), low densities (10^2–10^4 cm^{-3}), and in intense radiation fields. We have previously proposed that the structure and reactivity of mass-selected and temperature-controlled gas-phase clusters consisting of interstellar and biological molecules are important for understanding the chemical processes in interstellar molecular clouds. Thus, we developed a tandem mass spectrometer containing a cold ion trap (8–350 K) for photodissociation spectroscopy of gas-phase clusters as a model for molecular clouds [23], and have previously reported the ultraviolet (UV) photodissociation of temperature-controlled gas-phase tryptophan (Trp) enantiomers on a chiral crown ether [23, 24], in L-serine (L-Ser) clusters [25, 26], and with L-alanine peptides [27].

Enantioselective photodissociation of gas-phase protonated tryptophan (H^+Trp) enantiomers, having NH_3^+ and COOH groups, in noncovalent gas-phase complexes with a chiral crown ether has been examined as a function of temperature [23, 24]. Photo-induced hydrogen atom transfer produced C_α–C_β bond cleavage in cold H^+(D-Trp) on the chiral crown ether. This C_α–C_β bond cleavage was increasingly suppressed with increasing temperature above 170 K, and no difference in reactivity was observed between the D- and L-enantiomers of H^+Trp at 300 K. These temperatures correspond to those of interstellar to atmospheric molecular clouds. The UV photodissociation of cold gas-phase Trp enantiomers in protonated L-serine clusters H^+(L-Ser)$_m$, as a function of cluster size m, showed that when three L-Ser units are present in the cluster, the photodissociation of Trp is enantioselective [25]. These enantioselective dissociations are due to the transmission of chirality from one type of molecule to another via photodissociation in gas-phase clusters. We have also applied enantioselective photodissociation to the quantitative chiral analysis of Trp in solution [24, 26]. Enantioselective photodissociation of Trp in gas-phase clusters generated using electrospray ionization was utilized to determine the enantiomeric excess of Trp in solution.

In this study, we examined chiral recognition and chiral transmission between monosaccharides and amino acids by UV photodissociation of cold gas-phase noncovalent complexes of glucose (Glc) and galactose (Gal) with H^+(L-Trp). L-Trp was used as a probe for chiral recognition and chiral transmission in the noncovalent complexes because cold gas-phase Trp shows enantioselective photodissociation when noncovalently complexed with the appropriate chiral substances as previously reported by our group [23–27]. We then applied this phenomenon to enantiomeric excess determination for monosaccharides.

Experimental

D-Glc, L-Glc, D-Gal, L-Gal, and L-Trp (all >98%) were obtained from Nacalai Tesque. A solution containing 1.0 mM of monosaccharide and 0.5 mM of L-Trp in a mixture of water and methanol (50/50, v/v) with 1% acetic acid was used.

Details of the lab-fabricated tandem mass spectrometer have been described previously [23]. It is comprised of an electrospray ionization source, an octopole ion guide, a quadrupole mass filter, a variable-temperature 22-pole ion trap, and a reflectron time-of-flight (TOF) mass spectrometer. Noncovalent gas-phase complexes of monosaccharide enantiomers with H^+(L-Trp) were generated using electrospray ionization, and transferred to the gas phase through a stainless steel capillary, a skimmer, and an octopole ion guide. The ionization source was operated at an applied voltage on a stainless steel needle tip (i.d. 0.1 mm) of 1.5 kV, a sample flow rate of 3 μL/min, and a nitrogen nebulizing gas flow rate of 4 L/min. The capillary was grounded and heated to 340 K. The gas-phase ions were deflected by 90° using an electrostatic quadrupole ion bender, mass-selected using a quadrupole mass filter, and temperature-controlled at 8 K using a 22-pole ion trap. The trap consisted of a pair of rf stainless steel electrodes with 11 rods each, cylindrical electrodes, and a copper housing. The trap assembly was mounted onto the second stage (8 K) of a cryogenic refrigerator (CH-204SB; Sumitomo), and was enclosed within an aluminum radiation shield in thermal contact with the first stage (50 K). The trap temperature was measured by two silicon diode temperature sensors (DT-670B-CU; LakeShore). In the trap, the ions were thermalized by multiple collisions with the He buffer gas contained within the copper housing at a well-defined temperature, analogous to a thermal bath. The mass-selected and temperature-controlled ions were extracted from the trap and then irradiated with a photodissociation laser pulse. The fragment ions were orthogonally accelerated to 2.8 kV, and then mass-analyzed using a reflectron TOF mass spectrometer. The ion signals were counted using dual microchannel plates (F4655; Hamamatsu) and stored in a digital storage oscilloscope (6100A; LeCroy) after being amplified using a wide-band amplifier (BX-31; NF Electronic Instruments). The repetition rate of the experimental cycle was 10 Hz. The fourth harmonic of a Nd:YAG laser (Minilite II; Continuum) was used as the photodissociation light, the pulse width of which was 4 ns. The wavelength was 266 nm, and the energy was around 1.5 mJ/pulse.

Results and Discussion

Chiral Transmission in Photodissociation

Figure 1 shows the photodissociation mass spectra of heterochiral H^+(L-Trp)(D-Glc) and homochiral H^+(L-Trp)(L-Glc) (*m/z* 385), which are protonated 1:1 noncovalent complexes, at 8 K. The irradiation wavelength was 266 nm, which excites the indole ring of L-Trp to the ππ* state. The monosaccharides do not absorb the excitation UV light. Glc evaporation, forming H^+(L-Trp) (*m/z* 205), is observed in both spectra. The proton in the noncovalent complexes remains associated with L-Trp. For heterochiral H^+(L-Trp)(D-Glc), as shown in Fig. 1a, C_α–C_β bond cleavage of L-Trp is observed at *m/z* 311

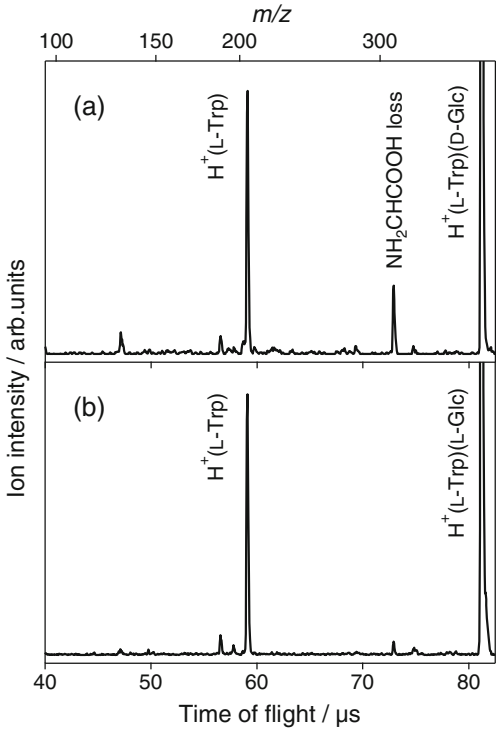

Figure 1. Photodissociation mass spectra of (**a**) H^+(L-Trp)(D-Glc) and (**b**) H^+(L-Trp)(L-Glc) (*m/z* 385) at 8 K. The irradiation wavelength was 266 nm, which excites the indole ring of L-Trp to the ππ* state

and 131. The C_α–C_β bond cleavage was reported to occur in UV photoexcitation of protonated tryptophan, where hydrogen atom transfer played an important role in it [23, 27, 28]. The product ion at *m/z* 311 is proposed to be $NH_2CHCOOH$ loss from heterochiral H^+(L-Trp)(D-Glc). This represents dissociation of L-Trp in a noncovalent complex. The dissociation of the noncovalent complex is not observed for homochiral H^+(L-Trp)(L-Glc), for which Glc evaporation is the main pathway. $NH_2CHCOOH$ loss due to C_α–C_β bond cleavage of L-Trp is enantioselective photodissociation induced by chiral recognition with D-Glc in the noncovalent complex. In the case when D-Trp was used as a probe, the photodissociation mass spectra of heterochiral H^+(D-Trp)(L-Glc) and homochiral H^+(D-Trp)(D-Glc) were identical to those shown in Fig. 1 for heterochiral H^+(L-Trp)(D-Glc) and homochiral H^+(L-Trp)(L-Glc), respectively.

L-Trp dissociates via C_α–C_β bond cleavage when noncovalently complexed with D-Glc. In contrast, no dissociation of L-Trp occurs in homochiral H^+(L-Trp)(L-Glc), where the energy absorbed by L-Trp is released through the evaporation of L-Glc. This enantioselective photodissociation of Trp is due to the transmission of chirality from Glc to Trp via photodissociation in the noncovalent complexes. The enantiomeric enrichment for the Trp enantiomer obtained via enantioselective photodissociation is 4.5% under these experimental conditions, which is derived from the ion intensities shown in Fig. 1. This type of chiral transmission to Trp was also observed for UV photodissociation of amino acid clusters [25, 26], as mentioned in the introduction. To be consistent with the homochirality in biomolecules consisting of L-amino acids and D-sugars, enantioselective photodissociation of Trp can occur in homochiral noncovalent complexes with Glc. For example, photodissociation of D-Trp inducing enantiomeric enrichment of L-Trp can occur when noncovalently complexed with D-Glc. However, enantioselective photodissociation of Trp occurred in heterochiral cold gas-phase protonated 1:1 noncovalent complexes with Glc, as in the case of amino acid clusters [25, 26]. To reveal the origins of enantiomeric enrichment in L-amino acids and D-sugars, other factors should be examined systematically, such as cluster size, temperature, solvation, excitation method, and behavior in solution.

UV photodissociation experiments with Gal enantiomers complexed with H^+(L-Trp) were also performed. Figure 2 shows the photodissociation mass spectra of heterochiral H^+(L-Trp)(D-Gal) and homochiral H^+(L-Trp)(L-Gal) (*m/z* 385) at 8 K. Gal evaporation forming H^+(L-Trp) is observed in both spectra, and $NH_2CHCOOH$ loss due to C_α–C_β bond cleavage of L-Trp is observed only for heterochiral H^+(L-Trp)(D-Gal), as is observed with Glc. The results suggest that chiral transmission between monosaccharides and amino acids occurs via photodissociation in the gas phase.

Enantiomeric Excess Determination

The differences between the D- and L-enantiomers in the photodissociation mass spectra can be used to determine enantiomeric excess based on kinetic methods. The enantioselective

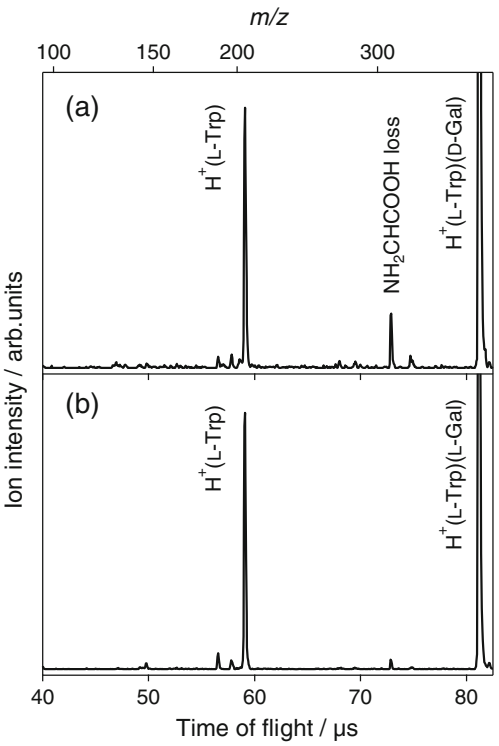

Figure 2. Photodissociation mass spectra of (**a**) H^+(L-Trp)(D-Gal) and (**b**) H^+(L-Trp)(L-Gal) (*m/z* 385) at 8 K. The irradiation wavelength was 266 nm

photodissociation of Trp induced by chiral transmission from monosaccharides was applied to enantiomeric excess determination of the monosaccharides in solution.

The kinetic methods for the enantiomeric analysis utilized low-energy multiple collision-induced dissociations in a room-temperature ion trap, where competitive evaporations of molecules from gas-phase trimeric metal-bound complexes were detected. The trimeric complexes consisted of a transition metal ion, two chiral reference ligands, and a chiral analyte such as amino acids [11], dipeptides [12], drugs [13], and monosaccharides [14, 15]. The kinetic method was based on the difference in the binding energies of the enantiomers. In the UV photodissociation of cold gas-phase noncovalent complexes, a single-nanosecond UV laser pulse excites Trp directly to its electronic excited state. Gas-phase noncovalent complexes were temperature-controlled using a cold ion trap (8 K). The excitation energies and temperatures of the noncovalent complexes, the key parameters in fragmentation, were precisely controlled. Entropic effects contribute to the population distribution of conformers in clusters at higher temperatures, which can influence the reactivity of amino acids [23, 24]. To restrict the population distribution for quantitative analysis, we performed photodissociation experiments at the lowest temperature of our apparatus in this work.

Photodissociation mass spectra of several enantiomeric mixtures of H^+(L-Trp)(Glc) were measured at 8 K, where the D-enantiomer mole fraction values of Glc were 0.00, 0.25, 0.50, 0.75, and 1.00. The mole fraction of L-Trp, used as a probe, was constant in the measurements. The relative ion intensity of $NH_2CHCOOH$ loss, observed in the photodissociation mass spectra for enantiomeric mixtures, decreases with decreasing D-enantiomer fraction of Glc in the mixture. Glc evaporation forming H^+(L-Trp) is observed in all spectra. The relative abundance ratio R, which is ($NH_2CHCOOH$-elimination product ion intensity)/(Glc-evaporated ion intensity), depends on the enantiomeric composition of Glc. Figure 3 shows the plot of the natural logarithm of R as a function of the D-enantiomer fraction of Glc in the mixture. The rate constants of the two competitive dissociation pathways relate to the ion intensities of the product ions, and the natural logarithm plot was used for chiral recognition using mass spectrometry-based techniques [11–15, 24, 26]. A linear relationship for ln(R) versus the D-enantiomer fraction of Glc is obtained, with a slope of 1.755, an intercept of –3.136, and a correlation coefficient (r^2) of 0.996. This indicates that the enantiomeric excess of Glc in solution can be determined by measuring R in a photodissociation mass spectrum and by referring to the linear relationship shown in Fig. 3.

In the case of Gal, shown in Fig. 2, R is derived by ($NH_2CHCOOH$-elimination product ion intensity)/(Gal-evaporated ion intensity). A linear relationship for ln(R) versus the D-enantiomer fraction of Gal in the mixture is obtained with a slope of 1.821, an intercept of –3.156, and an r^2 of 0.996, as shown in Fig. 4. These results indicate that photo-excited L-Trp can be used as a probe to determine the enantiomeric excess of monosaccharides in solution.

Conclusions

Chiral transmission between monosaccharides and amino acids via photodissociation in the gas phase was examined by UV photodissociation of cold gas-phase noncovalent complexes of Glc enantiomers with H^+(L-Trp), in which L-Trp was photo-excited. L-Trp dissociated via C_α–C_β bond cleavage when noncovalently complexed with D-Glc, whereas no dissociation of L-Trp occurred in homochiral H^+(L-Trp)(L-Glc). This enantioselective photodissociation of Trp is due to the transmission of chirality from Glc to Trp via photodissociation in the gas-phase noncovalent complexes.

The chiral transmission in photodissociation was applied to the quantitative chiral analysis of monosaccharides. The enantiomeric excess of monosaccharides in solution was determined by measuring the relative abundance ratio of the two product ions in a single photodissociation mass spectrum of cold gas-phase noncovalent complex with H^+(L-Trp) generated using electrospray ionization, and by referring to the linear relationships derived in this work. The excitation energy and the temperature of the gas-phase ions, which are key parameters for the fragmentation, were precisely controlled using a single-nanosecond laser pulse and a cold ion trap, respectively.

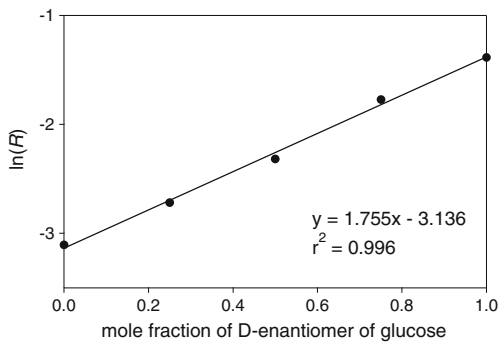

Figure 3. Linear relationship of ln(R) versus mole fraction of the D-enantiomer of Glc at 8 K for H^+(L-Trp)(Glc), where the relative abundance ratio R is ($NH_2CHCOOH$-elimination product ion intensity)/(Glc-evaporated ion intensity)

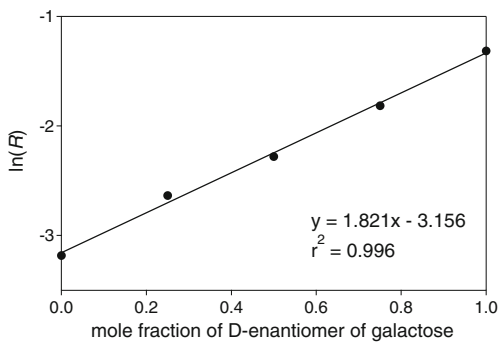

Figure 4. Linear relationship of ln(R) versus mole fraction of the D-enantiomer of Gal at 8 K for H^+(L-Trp)(Gal), where the relative abundance ratio R is ($NH_2CHCOOH$-elimination product ion intensity)/(Gal-evaporated ion intensity)

This method has several advantages over conventional techniques, including its device independence due to the well-defined excitation energy and temperature, no requirement for a chromophore in the analyte due to L-Trp being used as a probe, nonreliance on isotopic labeling, independence of the relative concentrations of the analyte and the probe molecule, and insensitivity to impurities.

Many asymmetric syntheses and kinetic methods measurements commonly use transition metals. The enantioselective photodissociation in this work is a transition-metal-free asymmetric reaction. Asymmetric syntheses without transition-metal-based catalysis have been developed extensively, and are important in green sustainable chemistry [29]. The structures determined by inter- and intra-molecular hydrogen bonds in the noncovalent complexes are important for understanding the chiral recognition, chiral transmission via photodissociation, and transition-metal-free asymmetric reactions, in addition to chemical evolution in molecular clouds. To reveal the geometrical structures, it is necessary to perform photodissociation spectroscopy and make direct comparisons with the theoretical calculations for mass-selected and temperature-controlled gas-phase noncovalent complexes.

References

1. McConnell, O., Bach, A., Balibar, C., Byrne, N., Cai, Y., Carter, G., Chlenov, M., Di, L., Fan, K., Goljer, I., He, Y., Herold, D., Kagan, M., Kerns, E., Koehn, F., Kraml, C., Marathias, V., Marquez, B., McDonald, L., Nogle, L., Petucci, C., Schlingmann, G., Tawa, G., Tischler, M., Williamson, R.T., Sutherland, A., Watts, W., Young, M., Zhang, M.-Y., Zhang, Y., Zhou, D., Ho, D.: Enantiomeric separation and determination of absolute stereochemistry of asymmetric molecules in drug discovery—building chiral technology toolboxes. Chirality **19**, 658–682 (2007)
2. Ward, T.J., Ward, K.D.: Chiral separations: a review of current topics and trends. Anal. Chem. **84**, 626–635 (2012)
3. Scriba, G.K.E.: Chiral recognition mechanisms in analytical separation sciences. Chromatographia **75**, 815–838 (2012)
4. Nagata, H., Machida, Y., Nishi, H., Kamigauchi, M., Minoura, K., Ishida, T.: Structural requirement for chiral recognition of amino acid by (18-Crown-6)-tetracarboxylic acid: binding analysis in solution and solid states. Bull. Chem. Soc. Jpn. **82**, 219–229 (2009)
5. Zehnacker, A., Suhm, M.A.: Chirality recognition between neutral molecules in the gas phase. Angew. Chem. Int. Ed. **47**, 6970–6992 (2008)
6. Shizuma, M., Ohta, M., Yamada, H., Takai, Y., Nakaoki, T., Takeda, T., Sawada, M.: Enantioselective complexation of chiral linear hosts containing monosaccharide moieties with chiral organic amines. Tetrahedron **58**, 4319–4330 (2002)
7. Shizuma, M., Kadoya, Y., Takai, Y., Imamura, H., Yamada, H., Takeda, T., Arakawa, R., Takahashi, S., Sawada, M.: New artificial host compounds containing galactose end group for binding chiral organic amine guests: chiral discrimination and their complex structures. J. Org. Chem. **67**, 4795–4807 (2002)
8. Sawada, M.: Chiral recognition detected by fast atom bombardment mass spectrometry. Mass Spectrom. Rev. **16**, 73–90 (1997)
9. Schalley, C.A.: Molecular recognition and supramolecular chemistry in the gas phase. Mass Spectrom. Rev. **20**, 253–309 (2001)
10. Awad, H., El-Aneed, A.: Enantioselectivity of mass spectrometry: challenges and promises. Mass Spectrom. Rev. **32**, 466–483 (2013)
11. Tao, W.A., Zhang, D., Nikolaev, E.N., Cooks, R.G.: Copper(II)-assisted enantiomeric analysis of D,L-amino acids using the kinetic method: chiral recognition and quantification in the gas phase. J. Am. Chem. Soc. **122**, 10598–10609 (2000)
12. Tao, W.A., Cooks, R.G.: Parallel reactions for enantiomeric quantification of peptides by mass spectrometry. Angew. Chem. Int. Ed. **40**, 757–760 (2001)
13. Tao, W.A., Gozzo, F.C., Cooks, R.G.: Mass spectrometric quantitation of chiral drugs by the kineitc method. Anal. Chem. **73**, 1692–1698 (2001)
14. Nagy, G., Pohl, N.L.B.: Monosaccharide identification as a first step toward de novo carbohydrate sequencing: mass spectrometry strategy for the identification and differentiation of diastereomeric and enantiomeric pentose isomers. Anal. Chem. **87**, 4566–4571 (2015)
15. Nagy, G., Peng, T., Pohl, N.L.B.: General label-free mass spectrometry-based assay to identify glycosidase substrate competence. Anal. Chem. **88**, 7183–7190 (2016)
16. Fuke, K., Tona, M., Fujihara, A., Sakurai, M., Ishikawa, H.: Design and development of a novel nuclear magnetic resonance detection for the gas phase ions by magnetic resonance acceleration technique. Rev. Sci. Instrum. **83**(1–8), 085106 (2012)
17. Fuke, K., Ohshima, Y., Tona, M.: Preparation of cold ions in strong magnetic field and its application to gas-phase NMR spectroscopy. Hyper. Inter. **236**, 9–18 (2015)
18. Pizzarello, S., Groy, T.L.: Molecular asymmetry in extraterrestrial organic chemistry: an analytical perspective. Geochim. Cosmochim. Acta **75**, 645–656 (2011)
19. Meinert, C., Marcellus, P.d., d'Hendecourt, L.L.S., Nahon, L., Jones, N.C., Hoffmann, S.V., Bredehöft, J.H., Meierhenrich, U.J.: Photochirogenesis: photochemical models on the absolute asymmetric formation of amino acids in interstellar space. Phys. Life Rev. **8**, 307–330 (2011)
20. Abplanalp, M.J., Förstel, M., Kaiser, R.I.: Exploiting single photon vacuum ultraviolet photoionization to unravel the synthesis of complex organic molecules in interstellar ices. Chem. Phys. Lett. **644**, 79–98 (2016)
21. McGuire, B.A., Carroll, P.B., Loomis, R.A., Finneran, I.A., Jewell, P.R., Remijan, A.J., Blake, G.A.: Discovery of the interstellar chiral molecule propylene oxide (CH_3CHCH_2O). Science **352**, 1449–1452 (2016)
22. Nanita, S.C., Cooks, R.G.: Serine octamers: cluster formation, reactions, and implications for biomolecule homochirality. Angew. Chem. Int. Ed. **45**, 554–569 (2006)
23. Fujihara, A., Sato, T., Hayakawa, S.: Enantiomer-selective ultraviolet photolysis of temperature-controlled protonated tryptophan on a chiral crown ether in the gas phase. Chem. Phys. Lett. **610**(611), 228–233 (2014)
24. Fujihara, A., Maeda, N., Hayakawa, S.: Quantitative chiral analysis of tryptophan using enantiomer-selective photolysis of cold non-covalent complexes in the gas phase. J. Mass Spectrom. **50**, 451–453 (2015)
25. Fujihara, A., Maeda, N., Hayakawa, S.: Enantiomer-selective photolysis of cold gas-phase tryptophan in L-serine clusters with linearly polarized light. Orig. Life Evol. Biosph. **44**, 67–73 (2014)
26. Fujihara, A., Maeda, N., Hayakawa, S.: Enantioselective photolysis and quantitative chiral analysis of tryptophan complexed with alkali-metalized L-serine in the gas phase. Chirality **27**, 349–352 (2015)
27. Fujihara, A., Maeda, N., Hayakawa, S.: Chiral recognition between L-alanine peptides and tryptophan enantiomers probed by ultraviolet photodissociation in the gas phase. J. Mass Spectrom. **51**, 257–260 (2016)
28. Grégoire, G., Lucas, B., Barat, M., Fayeton, J.A., Dedonder-Lardeux, C., Jouvet, C.: UV photoinduced dynamics in protonated aromatic amino acid. Eur. Phys. J. D. **51**, 109–116 (2009)
29. List, B.: Proline-catalyzed asymmetric reactions. Tetrahedron **58**, 5573–5590 (2002)