Hydration of serine–metal cation complexes: implication for the role of water in the origin of homochirality on the Earth

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Abstract

It may be taken for granted that the processes that occurred in water were of crucial importance for the origin of life. Therefore, it is quite likely that water was also important with respect to the origin of homochirality. Here, it is shown, using electrospray ionization mass spectrometry, that the efficiency of hydration of homochiral serine–metal cation complexes is different from that of heterochiral serine–metal cation complexes. The differences in the efficiency of hydration of homo and heterochiral metal cation–amino acid complexes could lead to the amplification of formation of homochiral peptides in water solution from which life emerged.

Keywords Serine · Metal complexes · Hydration · Electrospray ionization · Mass spectrometry

Introduction

The problem of the origin of homochirality in living systems has been widely discussed. There are theories assuming that serine could play an important role in this matter (Ávalos et al. 2010; Blackmond and Klussmann 2007; Cintasi and Viedma 2012; Klussmann and Blackmond 2009; Kojo 2010; Ruiz-Mirazo et al. 2014; Toxvaerd 2009). The serine role could be related to the following findings: serine exhibits a eutectic point of > 99% enantiomeric excess—ee (Klussmann et al. 2006), sublimation of serine with the initial ee of 3% yielded sublimates of 68–92% ee (Perry et al. 2007), and under some specific conditions (e.g., electrospray ionization conditions) serine yields stable preferentially homochiral octamer (Cooks et al. 2001; Nanita and Cooks 2006), although it has to be added that serine octamer does not exist in solution (Vandenbussche et al. 2006). Water is the most fundamental compound indispensable for life existence on the Earth (it is almost truism).

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One of the most interesting theories of the origin of life is those that life emerged in the so-called warm little pond (Peretó et al. 2009) or in the so-called prebiotic soup (Bada and Lazcano 2003)—both were water solutions. It may be taken for granted that the processes that occurred in water were of crucial importance for the origin of life. Therefore, it is quite likely that water was also important with respect to the origin of homochirality. Here it is shown, by using electrospray ionization mass spectrometry, that the efficiency of hydration of homochiral serine–metal cation complexes is different from that of heterochiral serine–metal cation complexes. In the water solution from which life emerged, there must have been simple chiral molecules and metal cations and they formed complexes which were hydrated. It is obvious that hydration process affected the formation of larger biomolecules.

Materials and methods

Serine (SerL and SerD) and isotope-labeled serine (SerL-¹³C₃, 98% ¹³C, 95% CP, Scheme 1) were obtained from Sigma-Aldrich (Poznań, Poland) and used without further purification.

The product ion spectra (CID-MS/MS spectra) were taken on a Waters/Micromass (Manchester, UK) Q-tof Premier mass spectrometer (software MassLynx V4.1, Manchester, UK). The sample solutions were prepared in methanol

Scheme 1 Structure of isotope-labeled L-serine¹³C₃—molecular weight 108 (left) and D-serine—molecular weight 105 (right)

(the most common solvent for electrospray ionization) with concentrations of serine and inorganic salt of 10^{-4} mol/dm³ (concentration refers to the each ingredient, not to the sum). The sample solutions were infused into the ESI source by a syringe pump at a flow rate of 5 µl/min. The electrospray voltage was 2.7 kV and the cone voltage was 30 V. The source temperature was 80 °C and the desolvation temperature was 250 °C. Nitrogen was used as the cone gas and desolvating gas at the flow rates of 0.8 and 13 dm³/min, respectively. Argon 4.0 was used as a collision gas at the flow rate 0.2–0.6 ml/min (0.2 is the standard value) in the T-wave collision cell. The relation between the collision gas flow rate and the collision cell pressure has been published elsewhere (Frański 2019). Collision energy (the most important parameter for CID-MS/MS experiments) was 5–20 eV—laboratory frame. Exemplary product ion spectra obtained at different collision energies are shown in Supplementary Materials (Figs. 1s, 2s).

Scan time was 0.5 s, inter scan time was 0.1 s and run duration was 6 s. Thus, each point at the breakdown plots was generated by averaging ten mass spectra. The calculated relative standard deviations did not exceed 5%.

Usually, to study the gas phase interaction between water molecule (and other solvent molecule) and ion, the use of a specially designed mass spectrometer is required. However, sometimes the interaction between ions and water which is present as an impurity in the commercial mass spectrometers may be also very interesting (Alechaga et al. 2016; Beach and Gabryelski 2018; Frański 2019; Hu et al. 2017). It is evident that the attached water comes from the collision gas, in which it is present as an impurity, since the collision gas flow rate strongly affected the ratios $[(\text{SerL-H})_3\text{Ca}_2 + \text{H}_2\text{O}]^+ / [(\text{SerL-H})_3\text{Ca}_2]^+$ (m/z 410 and 392, Supplementary Material Fig. 3s) and $[(\text{SerL-H})_3\text{Mg}_2 + \text{H}_2\text{O}]^+ / [(\text{SerL-H})_3\text{Mg}_2]^+$ (m/z 378 and 360, Supplementary Material—Fig. 4s).

Because of a wide window, the ion beam selected for MS/MS experiment contained all abundant ions generated from the solution of SerL¹³C₃ and SerD (or SerL¹³C₃ and SerL). It was very important for the purpose of this work, since in this way the hydration of homochiral and heterochiral ions occurred in one MS/MS experiment, thus in identical conditions (!). It is well known that the mass spectra obtained at some time interval (in identical instrumental conditions)

may be different because of the fluctuations of pressure inside the mass spectrometer (David and Brodbelt 2003).

Results and discussion

If we deal with a racemic solution, it is difficult to find if there are any species being enantioenriched, without their prior isolation. Electrospray ionization mass spectrometry (ESI-MS) is a well-known method of transfer of ions from solution to the gas phase. Then, the properties of each of the obtained ion in the gas phase may be further studied by its collision-induced dissociation (CID-MS/MS) and/or by ion–molecule reaction, e.g., hydration.

From the solution containing serine (Ser) and Ca(NO₃)₂, the ion $[(\text{Ser-H})_3\text{SerCa}_2]^+$ at m/z 497 was obtained using ESI-MS. For a racemic solution containing D-serine (SerD), isotope-labeled L-serine¹³C₃ and Ca(NO₃)₂, the respective isotope-labeled ions were obtained. Upon CID conditions, product ions $[(\text{Ser-H})_3\text{Ca}_2]^+$ were formed from the precursor ions $[(\text{Ser-H})_3\text{SerCa}_2]^+$ (loss of serine molecule). The formed product ions have attached water molecules (water was present in the collision cell as an impurity). As clearly shown in Fig. 1, water attachment to the heterochiral complexes (product ions $[(\text{SerL}^{13}\text{C}_3\text{-H})_2(\text{SerD-H})\text{Ca}_2]^+$ at m/z 398 and $[(\text{SerL}^{13}\text{C}_3\text{-H})(\text{SerD-H})_2\text{Ca}_2]^+$ at m/z 395) is more efficient than water attachment to the homochiral complexes (product ions $[(\text{SerL}^{13}\text{C}_3\text{-H})_3\text{Ca}_2]^+$ at m/z 401 and $[(\text{SerD-H})_3\text{Ca}_2]^+$ at m/z 392).

For magnesium-containing ions (obtained from racemic solution containing SerD, SerL¹³C₃ and Mg(NO₃)₂), the opposite situation was observed. Namely, water attachment to the homochiral complexes (product ions $[(\text{SerL}^{13}\text{C}_3\text{-H})_3\text{Mg}_2]^+$ at m/z 369 and $[(\text{SerD-H})_3\text{Mg}_2]^+$ at m/z 360) was more efficient than water attachment to the heterochiral complexes (product ions $[(\text{SerL}^{13}\text{C}_3\text{-H})_2(\text{SerD-H})\text{Mg}_2]^+$ at m/z 366 and $[(\text{SerL}^{13}\text{C}_3\text{-H})(\text{SerD-H})_2\text{Mg}_2]^+$ at m/z 363), as clearly seen in Fig. 2.

In order to be sure that the found differences between hydration of homochiral and heterochiral complexes (Figs. 1, 2) are not accidental or are not caused by apparatus effects, the respective MS experiments were performed for complexes containing SerL¹³C₃ and SerL. As expected, the efficiency of hydration of all ions containing SerL¹³C₃ and/or SerL was very similar (Supplementary Material, Figs. 5s, 6s).

The most common divalent metals on Earth are iron, calcium and magnesium. Therefore, hydration of serine–Fe complexes was studied as well. However, the efficiency of their hydration was low (Supplementary Material, Fig. 7s) in comparison to the hydration of serine–Ca and serine–Mg complexes.

Fig. 1 Exemplary product ion spectrum of isotope-labeled ions $[(\text{Ser-H})_3\text{SerCa}_2]^+$, $\text{SerL}^{13}\text{C}_3/\text{SerD } 3/1$ — m/z 506 (e.g., $[(\text{SerL}^{13}\text{C}_3\text{-H})_3(\text{SerD-H})\text{Ca}_2]^+$); $\text{SerL}^{13}\text{C}_3/\text{SerD } 2/2$ — m/z 503; $\text{SerL}^{13}\text{C}_3/\text{SerD } 1/3$ — m/z 500 and the breakdown plots of the ratio of ion abundances against the collision gas flow rate. It is evident that hydration of heterochiral complexes is more efficient than hydration of homochiral complexes

Divalent metal cation could enhance the prebiotic formation of the first peptides from amino acids (Beck 2011; Kitadai et al. 2011; Remko and Rode 2004). The differences in the efficiency of hydration of homo and heterochiral metal cation–amino acid complexes undoubtedly led to the amplification of formation of homochiral peptides in water solution from which life emerged. The open question is if the higher efficiency of hydration of homochiral complexes than heterochiral complexes (Mg complexes) enhanced the formation of homochiral peptides or the lower efficiency of hydration of homochiral complexes than heterochiral complexes (Ca complexes) enhanced the formation of homochiral peptides.

It is worth mentioning that hydration of 1:1 amino acid–metal cation complexes has been widely studied

(Burt and Fridgen 2013; Gholami and Fridgen 2013; Jockusch et al. 2001; Lemoff et al. 2006; Wincel 2007a, b). However, the influence of chirality on hydration of complexes characterized by high stoichiometry surely needs further investigation.

It is also worth mentioning that meteorites contain enantiomeric excess of amino acids (Glavin et al. 2012; Pizzarello and Yarnes 2016). These findings may be regarded as being against the argument that the processes occurring in water on Earth are responsible for the homochirality. However, it is reasonable to assume that not only one process could lead to the enantioenrichment. Furthermore, it cannot be definitely excluded that the origin of enantiomeric excess in meteorites is related to the process occurring in water.

Fig. 2 Exemplary product ion spectrum of isotope-labeled ions $[(\text{Ser-H})_3\text{SerMg}_2]^+$ (characteristic isotope pattern of magnesium-containing ions is clearly seen). $\text{SerL}^{13}\text{C}_3/\text{SerD}$ 3/1— m/z 474 (e.g., $[(\text{SerL}^{13}\text{C}_3\text{-H})_3(\text{SerD-H})\text{Mg}_2]^+$); $\text{SerL}^{13}\text{C}_3/\text{SerD}$ 2/2— m/z 471; $\text{SerL}^{13}\text{C}_3/\text{SerD}$ 1/3— m/z 468 and the breakdown plots of the ratio of ion abundances against the collision gas flow rate. It is evident that the hydration of homochiral complexes is more efficient than the hydration of heterochiral complexes

Another problem is that amino acids may be racemized in water. Furthermore, the metal cations may enhance the racemization of amino acids (Reddy et al. 1989; Smith et al. 1983; Stadtherr and Angelici 1975). However, the metal cations which enhance the racemization of amino acids are transition metal cations. Alkali earth metal cations have not been found to possess such a property (alkali earth metal cations are not prone to be coordinated by amino group).

The RNA world hypothesis suggests that homochirality has to be related to the formation of RNA molecules containing D-ribose (Pressman et al. 2015; Tamura 2008). This hypothesis seems to question the role of amino acids in the origin of homochirality. However, highly enantioenriched RNA precursor molecules can be formed from a racemic mixture of precursors in the presence of amino acids containing very small enantiomeric excess (Hein et al. 2011).

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals.

Informed consent No informed consent is required for this study.

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References

- Alechaga É, Moyano E, Galceran MT (2016) Ion-molecule adduct formation in tandem mass spectrometry. *Anal Bioanal Chem* 408:1269–1277. <https://doi.org/10.1007/s00216-015-9237-6>
- Ávalos M, Babiano R, Cintas P, Jiménez JL, Palacios JC (2010) Homochirality and chemical evolution: new vistas and reflections on recent models. *Tetrahedron Asymmetry* 21:1030–1040. <https://doi.org/10.1016/j.tetasy.2010.03.049>
- Bada JL, Lazcano A (2003) Perceptions of science: prebiotic soup—revisiting the Miller experiment. *Science* 300:745–746. <https://doi.org/10.1126/science.1085145>
- Beach DG, Gabryelski W (2018) Solution to collision induced dissociation mass spectrometry challenge. *Anal Bioanal Chem* 410:3927–3930. <https://doi.org/10.1007/s00216-017-0684-0>
- Beck W (2011) Metal complexes of biologically important ligands, CLXXVI.^[1] Formation of peptides within the coordination sphere of metal ions and of classical and organometallic complexes and some aspects of prebiotic chemistry. *Z Anorg Allg Chem* 637:1647–1672. <https://doi.org/10.1002/zaac.201100137>
- Blackmond DG, Klusmann M (2007) Spoilt for choice: assessing phase behavior models for the evolution of homochirality. *Chem Commun* 2007:3990–3996. <https://doi.org/10.1039/B709314B>
- Burt MB, Fridgen TD (2013) Gas-phase structures of Pb²⁺-cationized phenylalanine and glutamic acid determined by infrared multiple photon dissociation spectroscopy and computational chemistry. *J Phys Chem A* 117:1283–1290. <https://doi.org/10.1021/jp306420e>
- Cintasi P, Viedma C (2012) On the physical basis of asymmetry and homochirality. *Chirality* 24:894–908. <https://doi.org/10.1002/chir.22028>
- Cooks RG, Zhang D, Koch KJ, Gozzo FC, Eberlin MN (2001) Chiroselective self-directed octamerization of serine: implications for homochirogenesis. *Anal Chem* 73:3646–3655. <https://doi.org/10.1021/ac010284i>
- David WM, Brodbelt JS (2003) Threshold dissociation energies of protonated amine/polyether complexes in a quadrupole ion trap. *J Am Soc Mass Spectrom* 14:383–392
- Frañski R (2019) Gas phase hydration of polyethylene glycol–metal cation complexes. *J Mass Spectrom* 54:88–91. <https://doi.org/10.1002/jms.4310>
- Gholami A, Fridgen TD (2013) Structures and unimolecular reactivity of gas-phase [Zn(Proline-H)]⁺ and [Zn(Proline-H)(H₂O)]⁺. *J Phys Chem B* 117:8447–8456. <https://doi.org/10.1021/jp404697g>
- Glavin DP, Elsila JE, Burton AS, Callahan MP, Dworkin JP, Hilts RH, Christopher DK (2012) Unusual nonterrestrial L-proteinogenic amino acid excesses in the Tagish Lake meteorite. *Meteorit Planet Sci* 47:1347–1364. <https://doi.org/10.1111/1745-5100.2012.01400.xg>
- Hein JE, Tse E, Blackmond DG (2011) A route to enantiopure RNA precursors from nearly racemic starting materials. *Nat Chem* 3:704–706. <https://doi.org/10.1038/nchem.1108>
- Hu D, Cai T, Wang W-Y, Ye L-M, Wu Z-J (2017) Unexpected hydrated ions in the detection of sodium adduct coumarins using electrospray tandem mass spectrometry. *Eur J Mass Spectrom* 23:122–126. <https://doi.org/10.1177/1469066717699217>
- Jockusch RA, Lemoff AS, Williams ER (2001) Hydration of valine–cation complexes in the gas phase: on the number of water molecules necessary to form a zwitterion. *J Phys Chem A* 105:10929–10942. <https://doi.org/10.1021/jp013327a>
- Kitadai N, Yokoyama T, Nakashima S (2011) Hydration–dehydration interactions between glycine and anhydrous salts: implications for a chemical evolution of life. *Geochim Cosmochim Acta* 75:6285–6299. <https://doi.org/10.1016/j.gca.2011.08.027>
- Klusmann M, Blackmond DG (2009) Origin of homochirality. *ACS Symp Ser* 1025:133–145. <https://doi.org/10.1021/bk-2009-1025.ch007>
- Klusmann M, Iwamura H, Mathew SP, Jr Wells DH, Pandya U, Armstrong A, Blackmond DG (2006) Thermodynamic control of asymmetric amplification in amino acid catalysis. *Nature* 441:621–623. <https://doi.org/10.1038/nature04780>
- Kojo S (2010) Origin of homochirality of amino acids in the biosphere. *Symmetry* 2:1022–1032. <https://doi.org/10.3390/sym2021022>
- Lemoff AS, Wu C-C, Bush MF, Williams ER (2006) Binding energies of water to doubly hydrated cationized glutamine and structural analogues in the gas phase. *J Phys Chem A* 110:3662–3669. <https://doi.org/10.1021/jp055662v>
- Nanita SC, Cooks RG (2006) Serine octamers: cluster formation, reactions, and implications for biomolecule homochirality. *Angew Chem Int Ed* 45:554–569. <https://doi.org/10.1002/anie.200501328>
- Peretó J, Bada JL, Lazcano A (2009) Charles Darwin and the origin of life. *Orig Life Evol Biosph* 39:395–406. <https://doi.org/10.1007/s11084-009-9172-7>
- Perry RH, Wu C, Neffiu M, Cooks RG (2007) Serine sublimates with spontaneous chiral amplification. *Chem Commun* 2007:1071–1073. <https://doi.org/10.1039/B616196K>
- Pizzarello S, Yarnes CT (2016) Enantiomeric excesses of chiral amines in ammonia-rich carbonaceous meteorites. *Earth Planet Sci Lett* 443:176–184. <https://doi.org/10.1016/j.epsl.2016.03.021>
- Pressman A, Blanco C, Chen IA (2015) The RNA world as a model system to study the origin of life. *Curr Biol* 25:R953–R963. <https://doi.org/10.1016/j.cub.2015.06.016>
- Reddy GS, Reddy GV, Smith GG (1989) The effect of Ni(II), Zn(II), Cu(II), Co(II) and Pd(II) ions on racemisation of hydroxy α -amino acids. *Inorg Chim Acta* 166:55–58. [https://doi.org/10.1016/S0020-1693\(00\)80786-01](https://doi.org/10.1016/S0020-1693(00)80786-01)
- Remko M, Rode MM (2004) Catalyzed peptide bond formation in the gas phase. Role of bivalent cations and water in formation of 2-aminoacetamide from ammonia and glycine and in dimerization of glycine. *Struct Chem* 15:223–232. <https://doi.org/10.1023/B:STUC.0000021531.69736.00>
- Ruiz-Mirazo K, Briones C, De La Escosura A (2014) Prebiotic systems chemistry: new perspectives for the origins of life. *Chem Rev* 114:285–366. <https://doi.org/10.1021/cr2004844>
- Smith GG, Khatib A, Reddy GS (1983) Effect of nickel(II) and cobalt(III) and other metal ions on the racemization of free and bound L-alanine. *J Am Chem Soc* 105:293–295. <https://doi.org/10.1021/ja00340a026>
- Stadtherr LG, Angelici RJ (1975) Metal ion catalyzed racemization and α -proton exchange of N,N-dicarboxymethyl-D-phenylglycine. *Inorg Chem* 14:4925–4930. <https://doi.org/10.1021/ic50146a0414>

- Tamura K (2008) Origin of amino acid homochirality: relationship with the RNA world and origin of tRNA aminoacylation. *Biosystems* 92:91–98. <https://doi.org/10.1016/j.biosystems.2007.12.005>
- Toxvaerd S (2009) Origin of homochirality in biosystems. *Int J Mol Sci* 10:1290–1299. <https://doi.org/10.3390/ijms10031290>
- Vandenbussche S, Vandenbussche G, Reisse J, Bartik K (2006) Do serine octamers exist in solution? Relevance of this question in the context of the origin of homochirality on Earth. *Eur J Org Chem* 14:3069–3073. <https://doi.org/10.1002/ejoc.200600370>
- Wincel H (2007a) Hydration of potassiated amino acids in the gas phase. *J Am Soc Mass Spectrom* 18:2083–2089. <https://doi.org/10.1016/j.jasms.2007.09.006>
- Wincel H (2007b) Hydration energies of sodiated amino acids from gas-phase equilibria determinations. *J Phys Chem A* 111:5784–5791. <https://doi.org/10.1021/jp0721595>

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