Infrared spectrum and structure of the homochiral serine octamer-dichloride complex

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The amino acid serine is known to form a very stable octamer that has properties that set it apart from serine complexes of different sizes or from complexes composed of other amino acids. For example, both singly protonated serine octamers and anionic octamers complexed with two halogen ions strongly prefer homochirality, even when assembled from racemic $D_{,L}$ mixtures. Consequently, the structures of these complexes are of great interest, but no acceptable candidates have so far been identified. Here, we investigate anionic serine octamers coordinated with two chloride ions using a novel technique coupling ion mobility spectrometry-mass spectrometry with infrared spectroscopy, in combination with theoretical calculations. The results allow the identification of a unique structure for (Ser₈Cl₂)²⁻ that is highly symmetric, very stable and homochiral and whose calculated properties match those observed in experiments.

lusters of atoms or molecules with unusually high relative intensities in mass spectra are termed 'magic'. In many instances, these 'magic' clusters can be assigned to specific structures, often of high symmetry. Examples are numerous and include rare gas clusters¹ and fullerenes, most notably C_{60} (ref. 2), the Ti₈C₁₂ 'metallocarbohedrane'³, metal clusters such as Au₂₀ (refs 4,5), and highly symmetric protonated water clusters^{6,7}. In the case of C_{60} , the initial observation of magic numbers in mass spectra eventually led to the discovery of a new group of materials and a new form of carbon. Occasionally, a 'magic' cluster resists structural characterization. A famous example is the serine octamer. After electrospray of solutions containing serine, it was first observed that a cluster with the composition (Ser₈H)⁺ dominated the mass spectrum⁸. This is in contrast to mass spectra of other amino-acid clusters, for which the intensity patterns of peaks in their mass spectra show much smoother evolution⁹⁻¹⁴. Moreover, it was observed that when performing experiments with solutions containing a 50:50 mixture of L-serine and D-serine, the serine octamer defies statistics by strongly preferring homochiral clusters, that is, octamers that exclusively contain L-serine or D-serine¹⁵. Because of this unusual property, a possible link to the origin of homochirality in living organisms was made¹⁶. Besides $(Ser_8H)^+$, several other cationic serine octamer clusters, such as (Ser₈Na)⁺, were found to show 'magic' behaviour¹⁷. For anionic clusters, a deprotonated octamer has not been reported to show signs of special behaviour. However, octamer clusters containing two halide ions, such as $(Ser_8Cl_2)^{2-}$ and $(Ser_8Br_2)^{2-}$, are found to be abundant in mass spectra and, furthermore, are also observed to prefer homochirality¹⁸. For anionic clusters of other amino acids, special behaviour similar to that of $(Ser_8Cl_2)^{2-}$ or $(Ser_8Br_2)^{2-}$ is again not observed¹⁸.

Experimental observations have spurred calculations, and several candidates for the structures of cationic serine octamers have been proposed^{8,17,19-21}. However, for most of them, the proposed structures do not provide an obvious reason for the observed homochirality. In addition, although the calculations indicate that the proposed structures are stable, they are not dramatically more stable than serine clusters of different sizes. Thus, there is no

general consensus of the structure of serine octamer clusters and the quest for finding a structure that is compatible with the experimental observations is ongoing.

In contrast to the abundance of studies on the cationic serine octamer, little attention has so far been given to the anionic species. Here, we present results from a study on serine cluster anions in which we couple ion mobility spectrometry-mass spectrometry (IMS-MS) with infrared (IR) spectroscopy. IMS-MS gives the absolute, angle-averaged collision cross-section (CCS) of specific clusters, and this value can be used to determine the overall size of the cluster and to judge if particular calculated structures are compatible with experiments²²⁻²⁴. Furthermore, IMS-MS can be used to prepare samples for gas-phase IR spectroscopy²⁵⁻²⁹. Here, ions are simultaneously mass-to-charge (m/z) selected by MS, and specific oligomers are geometrically size selected by IMS. This is in contrast to experiments where only m/z selection is used, which can suffer from signal overlap between a cluster and its larger counterpart (which, for example, have twice the mass and twice the charge). While IMS provides information on the size and shape of a cluster, IR spectroscopy, especially in the fingerprint region (1,000-2,000 cm⁻¹), provides insights into the nature and interactions of functional groups in amino acids. IR spectroscopy without the use of IMS has been used to study the cationic protonated serine octamer with various substitutions in the X-H stretching region (X = N or O; $3,000-4,000 \text{ cm}^{-1}$), but has not yielded a definite structure for this complex^{30–32}. The focus of this study lies on $(Ser_8Cl_2)^{2-}$, for which a structure with high symmetry and stability is proposed. This structural assignment is supported by the experimental results as well by ab initio calculations, and we speculate that this complex might also exist in the condensed phase.

Results and discussion

Figure 1 presents time-of-flight (TOF) mass spectra as well as IMSresolved TOF mass spectra after electrospray of three serine samples. In Fig. 1a, the mass spectrum of an L-Ser sample is shown. The strongest peak occurs at m/z 455. Its drift time distribution (Fig. 1d) has a single peak that results from clusters with the composition (Ser₈Cl₂)²⁻, with no indication of the presence of isomers

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Figure 1 | **IMS-MS of serine cluster anions. a**-**c**, TOF mass spectra of aqueous solutions of L-Ser in HCI (**a**), a 1:1 mixture of L- and D-Ser in HCI (**b**) and a 1:1 mixture of D-Ser and L-Ser* in HCI, where L-Ser* is L-serine-D₃, ${}^{13}C_3$, ${}^{15}N_1$ (**c**). Notations: n^{z^-} stands for $[nSer+zCl]^{z^-}$; $(n+m)^{z^-}$ stands for $[(L-Ser^*)_n + (D-Ser)_m + z\cdotCl]^{z^-}$. The distributions of serine clusters complexed with two and three chloride ions are marked by dashed lines in the drift time versus m/z plots. **d-f**, Drift-time-selected TOF mass spectra highlighting octamer-dichloride complexes with three drift time windows: 5.8–6.0 ms (**I**), 6.3–6.5 ms (**II**) and 6.6–6.8 ms (**III**).

or higher oligomers (such as quadruply charged 16-mers). In the 2D plot in the lower part of Fig. 1a, all peaks for higher m/z species clearly group into different families that can be assigned to doubly and triply charged clusters. From the peaks in the drift time distributions, CCSs can be calculated and are provided in Supplementary Table 1. No clusters containing fewer than eight serine molecules are observed. The intensity of the cluster containing nine serine molecules is very weak, but larger clusters that range in composition from $(\text{Ser}_{10}\text{Cl}_2)^{2-}$ to $(\text{Ser}_{28}\text{Cl}_3)^{3-}$ are observed.

In Fig. 1b, the mass spectrum for a sample of 1:1 D-Ser and L-Ser is shown. Clearly, there are significant differences when compared with the enantiomerically pure sample in Fig. 1a. Most importantly, the relative intensities in the mass spectrum are different. The largest peak is now $(Ser_{10}Cl_2)^{2-}$, and the octamer $(Ser_8Cl_2)^{2-}$ has decreased in relative intensity. The drift time distribution for the octamer at m/z 455 has two peaks at drift times of ~5.9 ms and ~6.3 ms (labelled I and II, respectively) with the composition $(Ser_8Cl_2)^{2-}$, and cross-sections of 189 Å² and 201 Å², respectively.

An interesting question is how L- and D-Ser are distributed in the clusters for the 1:1 mixture. To answer this, experiments using D-Ser and isotopically labelled L-Ser^{*} (which is heavier by 7 AMU) were performed. The mass spectra and 2D plots are presented in Fig. 1c,f. The mass spectrum at the top of Fig. 1c shows broad peaks that arise from a heterogeneous distribution of L-Ser^{*} and D-Ser within each cluster. Most peaks appear to be symmetrical

and bell-shaped, suggestive of clusters with a statistical distribution of L-Ser^{*} and D-Ser. However, the distribution centred at m/z 469 is very different and does not have a bell shape. In the 2D drift time versus m/z plot in Fig. 1c, one can observe that several drift time peaks fall into that m/z region (labelled I, II and III). Peak I appears at the same drift time as peaks I in Fig. 1a,b and peak II at the same position as peak II in Fig. 1b. Peak III, on the other hand, is new. The mass spectra corresponding to drift time peaks I, II and III are shown in Fig. 1f. The mass spectrum for peak I shows a clearly non-statistical distribution of L-Ser* and D-Ser, with the maxima at m/z 455 and 483 corresponding to clusters where all eight Ser molecules are D-Ser (0+8) and L-Ser* (8+0), respectively. Next to the maxima are partially resolved and weaker peaks that correspond to the 1+7 and 7+1 clusters. Mass peaks that correspond to 2+6 (6+2), 3+5 (5+3) or 4+4 clusters are not observed for drift time peak I. (It should be noted that, for the case of a statistical assembly, the probability of randomly producing an 8+0 or 0+8 cluster is only 0.004, compared to a probability of 0.27 for the 4+4 cluster.) Peak II in Fig. 1f looks different from peak I and appears more bell-shaped, with a maximum at m/z469, corresponding to the 4+4 cluster. Peak III has a mass spectrum identical to peak II. This is strong evidence that this peak originates from loss of a Ser molecule from $(Ser_9Cl_2)^{2-}$ after the drift region, but before m/z selection. This is not unexpected given the apparently weak binding energy of a Ser molecule to the core

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Figure 2 | Size- and conformer-selected infrared spectra of serine cluster-dichloride complexes. **a**-**c**, Arrival time distributions and corresponding CCSs of $(Ser_{12}Cl_2)^{2^-}(\mathbf{a})$, $(Ser_{10}Cl_2)^{2^-}(\mathbf{b})$ and $(Ser_8Cl_2)^{2^-}(\mathbf{c})$. Red and blue traces denote the results from L-Ser only and racemic Ser, respectively. For $(Ser_8Cl_2)^{2^-}$, the smaller (CCS = 189 Å²) and larger (CCS = 201 Å²) conformers are annotated with I and II, respectively. **d**-**f**, Infrared spectra of $(Ser_{12}Cl_2)^{2^-}(\mathbf{d})$, $(Ser_{10}Cl_2)^{2^-}(\mathbf{e})$ and $(Ser_8Cl_2)^{2^-}(\mathbf{f})$. Grey dots are data points from two repeated scans and the lines denote averaged results. a.u., arbitrary units.

 $(Ser_8Cl_2)^{2-}$ cluster. The results from the IMS-MS experiment thus clearly show that when both L-Ser and D-Ser are present, $(Ser_8Cl_2)^{2-}$ strongly prefers a compact structure that is homochiral, in spite of the statistical improbability of this result. The statistically favoured non-homochiral structure (peak II) is formed as well, but its structure is different and significantly less compact. A non-homochiral isomer is also observed for the cationic protonated octamer³³; however, ion mobility experiments have not reported the presence of different isomers for those species^{20,21}.

To gain more insight into the structure of the serine octamer, we performed IR spectroscopy on $(Ser_8Cl_2)^{2-}$ as well as $(Ser_{10}Cl_2)^{2-}$ and $(Ser_{12}Cl_2)^{2-}$ using samples of both pure L-Ser and 1:1 chirally mixed L-Ser and D-Ser. The IR spectra of the m/z and drift time-selected species, together with the corresponding drift time distributions, are shown in Fig. 2. The red trace in Fig. 2c shows a drift time distribution of $(Ser_8Cl_2)^{2-}$ of pure L-Ser, where only a single peak is observed, as expected. The IR spectrum associated with this peak is shown in the lower red trace of Fig. 2f. The strongest IR band is found at 1,637 cm⁻¹, which has a shoulder at lower wavenumbers. Further strong bands are observed at 1,496 cm⁻¹, 1,382 cm⁻¹ and 1,059 cm⁻¹.

When a 1:1 L-Ser and D-Ser sample is sprayed, the drift time distribution for the m/z 455 channel, corresponding to $(\text{Ser}_8\text{Cl}_2)^{2-}$ contains two peaks and is shown as the blue trace in Fig. 2c. The CCS of peak I (189 Å²) is the same as for the peak in red for the pure L-Ser and is thus due to homochiral $(\text{Ser}_8\text{Cl}_2)^{2-}$. Peak II, on the other hand, originates from a less compact structure (CCS = 201 Å²), which is statistically assembled from L-Ser and D-Ser and is not homochiral. The IR spectra resulting from peaks I and II are shown in the two blue traces in Fig. 2f. The bands in the IR spectrum of the (Ser_8Cl_2)^{2-} ions that give rise to peak I occur at the same position and have a width comparable to those

observed in the spectrum of the pure L-Ser sample (in red). The spectrum for peak II, on the other hand, has bands at similar positions, but all of them are significantly broader. All IR spectra in Fig. 2 were taken using the same IR laser settings and hence any saturation effects or power broadening would affect all spectra in the same way.

Figure 2a,b presents drift time distributions for the larger clusters and Fig. 2d,e their corresponding IR spectra. In all drift time distributions, only a single peak is observed, and all their IR spectra are very similar and consist of broad bands, analogous to the spectrum for peak II of $(Ser_8Cl_2)^{2-}$.

A qualitative assignment of the spectra can give information on the structures of the clusters, even without performing quantum chemical calculations. For isolated amino acid molecules in the gas phase, structures with neutral carboxylic acid and amine groups are most stable. In aqueous solution, on the other hand, the zwitterionic form is more stable. To help answer the question of which form exists in the serine clusters, the vibrational modes of the carboxylic acid are most diagnostic. The band for the C=O stretch mode of a neutral carboxylic acid should occur for a free acid at \sim 1,780 cm⁻¹ (ref. 34) and shifts to 1,710 cm⁻¹ when strongly hydrogen-bonded to another acid³⁵ or 1,727 cm⁻¹ when coordinated to a Na⁺ ion³⁶. For a deprotonated carboxylic acid (carboxylate), on the other hand, the strong band for the antisymmetric stretching mode is found at 1,620-1,640 cm⁻¹ and the weaker band for the symmetric stretching mode is typically located at 1,300–1,400 cm⁻¹ (refs 37,38). In the IR spectra of all serine clusters investigated here (Fig. 2), the strongest band occurs at \sim 1,640 cm⁻¹ and no bands at higher wavenumber are observed, which implies that all carboxylic acid groups are deprotonated, all amine groups are protonated, and the molecules in all clusters are thus zwitterionic.

Most importantly, for homochiral $(Ser_8Cl_2)^{2-}$ all bands are narrow. This implies that all oscillators are in a similar environment and that the complex must have a highly symmetric structure. These narrow bands are in contrast to the IR spectra of the larger species $(Ser_{10}Cl_2)^{2-}$ and $(Ser_{12}Cl_2)^{2-}$ and heterochiral $(Ser_8Cl_2)^{2-}$ where the bands occur at similar positions, indicating zwitterionic species, but with significantly increased width. This broadening is almost certainly caused by local variations in the interactions of the oscillators with their surroundings, indicative of structures with low symmetry. Furthermore, for $(Ser_{10}Cl_2)^{2-}$ and $(Ser_{12}Cl_2)^{2-}$, there is no difference in cross-section (Fig. 2a,b) or IR spectra between enantiomerically pure and statistically mixed L- and D-Ser clusters. This indicates that $(Ser_{10}Cl_2)^{2-}$ and $(Ser_{12}Cl_2)^{2-}$, as well as heterochiral $(Ser_8Cl_2)^{2-}$, are non-specific assemblies of zwitterionic serine.

For $(Ser_8Cl_2)^{2-}$, a structure, for its compact form, must fulfil several requirements: (1) it has to have a strong preference for homochirality (that is, changing the chirality of one or more amino acid units destabilizes the structure); (2) the structure has to be compact and its calculated cross-section needs to match the experimental cross-section; (3) it has to consist purely of zwitterionic amino acid units; (4) the structure has to have an intrinsic preference for two chloride ions, not just one; (5) the stability should be exceptionally high and all possible hydrogen bonds should be saturated; (6) it should be specific to eight amino acid units and not easily add additional units; (7) the symmetry should be high in order to yield narrow bands in the IR spectrum; and (8) the theoretically calculated IR spectrum should match the experimental spectrum.

In principle, a global search for suitable structures that fulfil the above requirements can be carried out. However, because the conformation space is huge and accurate calculations of the energy are expensive, such an approach is impractical. We instead derived a structure guided by chemical intuition as well as by structures suggested previously^{8,19–21}. The resulting structure, optimized



Figure 3 | **Theoretical structure of the homochiral serine octamer-dichloride complex. a**, Proposed symmetric (D_4 point group) homochiral structure of the serine octamer-dichloride complex. The chloride anions are omitted from the chemical structure on the left for clarity, but shown on the right panel. The red arrows emphasize the two rings of four Ser molecules **b**, Theoretical infrared bands of the proposed structure compared with the experimental results. Symmetric and antisymmetric stretching vibrations (ν_{sym} and ν_{as}) of the carboxylate groups (-COO⁻) as well as deformations (δ) of protonated amine groups (-NH₃⁺) are assigned. Notations 'umb' and 'scis' indicate umbrella and scissoring modes. a.u., arbitrary units. **c,d**, Detailed views of the octamer from the side (**c**) and top (**d**). Atom colour code: C, grey; O, red; N, blue; H, white; Cl, green. The ionic size of the chloride anion is indicated by the larger pale green circle.

at the PBE0/cc-pVTZ level and including Grimme's D3 dispersion correction³⁹, is shown from several perspectives in Fig. 3. The structure is compact and has a theoretical CCS of 192 Å², which compares well to the experimental value for the homochiral species of 189 Å². All eight Ser molecules are equivalent by symmetry and the point group is D_4 . The structure can be thought of as consisting of two layers, with each layer consisting of a ring of four molecules that interact via hydrogen bonding of the -NH₃⁺ group and -OH side chain with the -COO⁻ group of the next molecule. Between the two layers, the sense of rotation is reversed and the two layers are secured to each other via -NH3⁺-OOC- salt bridges. The -NH3⁺ groups point slightly to the centre and form a cavity that holds the two chloride ions, whose distance from each other is only 3.96 Å (Fig. 3). The xyz coordinates of this structure are provided in Supplementary Table 2. The binding of the chloride ions is quite strong, and calculations show that the adiabatic removal of the first chloride ion requires 52 kcal mol⁻¹ of energy, and removal of both ions 169 kcal mol⁻¹. The Gibbs free energy of reaction (298 K) for gas-phase assembly of the structure from eight serine units and two chloride ions is calculated to be -106 kcal mol⁻¹ (Supplementary Tables 3 and 4).

Figure 3b shows the experimental IR spectrum of homochiral $(Ser_8Cl_2)^{2-}$ together with the calculated IR spectrum. Clearly, the match is very good in both peak positions and relative intensity. At the highest frequency of 1,639 cm⁻¹, the band for the asymmetric stretch mode of the $-COO^-$ group can be found, which is coupled to bending modes of the $-NH_3^+$ group. The three additional bands at 1,616 cm⁻¹, 1,583 cm⁻¹ and 1,496 cm⁻¹ arise from

bending modes in the $-NH_3^+$ group. The two strong bands slightly below 1,400 cm⁻¹ stem from the symmetric stretching modes of the $-COO^-$ group. Finally, a band is found at 1,070 cm⁻¹, which is redshifted to 1,059 cm⁻¹ in the experiment and arises from the C-OH stretch motions in the side chains. Experimental and theoretical IR spectra of (Ser₈Cl₂)²⁻ with isotopic substitutions further confirm the proposed structure (Supplementary Fig. 1).

The cluster structure shown in Fig. 3 has D_4 symmetry, in which all serine molecules are equivalent, and is the highest symmetry possible for a cluster of that composition. This also means that changing the chirality of one amino acid breaks the symmetry, leaves at least one functional group without a hydrogen-bonding partner, and disrupts the hydrogen-bonding pattern in one of the two rings. Changing the chirality of all four units in one of the rings changes its sense or rotation and thereby alters the interaction between those rings. Thus, the structure has a strong preference for homochirality. The high symmetry of the structure also implies that, because all monomer units are equivalent, all vibrational oscillators are equivalent as well, which explains why the bands in the IR spectrum are so narrow. The cavity in the structure is nicely suited to accept two negatively charged ions. The diameter of the cavity is \sim 4.25 Å, which is determined by the distance between two opposite hydrogen atoms of $-NH_3^+$ groups directed at the centre (Fig. 3c). In the equilibrium structure, the distance between two chloride ions is 3.96 Å. One can compare those values to the diameters of a chloride or bromide ion (~3.34 Å and ~3.64 Å, respectively⁴⁰) and conclude that the cavities are large enough to support those ions. An iodine ion on the other hand has an ionic diameter of 4.12 Å (ref. 40), too large to fit into the cavities without distorting them. This is in line with the observation of 'magic' $(\text{Ser}_8\text{Cl}_2)^{2-}$ and $(\text{Ser}_8\text{Br}_2)^{2-}$, but the absence of a corresponding iodine-containing counterpart¹⁸.

The structure for $(Ser_8Cl_2)^{2^-}$ is very special, and can only exist for serine and for clusters with eight monomer units. It does not offer suitable docking sites for the addition of further amino acid units, making the structure unreactive for further growth. An important question is to what degree can the structure of this anionic cluster be transferable to neutral or cationic clusters? Clearly, the size and electrostatic environment of the cavities are geared towards anions and, specifically, towards holding two of them. Removing those anions to generate a neutral structure will cause significant destabilization. For cationic species, the serine octamer is observed to be 'magic' either singly protonated or complexed with a single alkali ion. The anionic structure shown here will not easily accommodate those positive charges, and it is not clear if the cationic serine octamer complexes bear any resemblance to the anionic one.

Does the $(Ser_8Cl_2)^{2-}$ complex also exist in the condensed phase? A search for the protonated serine octamer in aqueous solution using IR and NMR was unsuccessful⁴¹. In the current experiment, ions were sampled via nano-electrospray ionization (nano-ESI). Provided that the experimental conditions are soft enough, even weakly bound complexes can be transferred to the gas phase and through the instrument. In the ESI process, complexes can assemble non-specifically during droplet evaporation, and disentangling these processes is generally difficult. There are, however, several points that speak against a non-specific assembly of the homochiral (Ser₈Cl₂)²⁻ cluster during the ESI process and indicate that this complex might very well exist in solution. First, in a non-specific aggregation scenario, smooth mass distributions would be expected, but the mass spectra (Fig. 1) do not show such behaviour. Second, fragmentation might occur during and after the ESI process. If this occurs, clusters containing fewer than eight serine units would be expected to be present, but they are not observed. Furthermore, we exclusively observe complexes containing two and three chloride ions; in a non-specific aggregation scenario, complexes containing just one chloride ion would be expected to be present as well. Although the above arguments are suggestive that homochiral (Ser₈Cl₂)²⁻ might be present in solution, they are not conclusive. Further studies are needed to unambiguously prove this special complex exists in solution.

Methods

Sample preparations. All solvents, hydrochloric acid, L-serine and D-serine were purchased from Sigma-Aldrich. L-Serine-2,3,3-D₃,¹³C₃,¹⁵N (L-Ser*) was obtained from Cambridge Isotope Laboratories. All sample solutions were prepared in water with a total serine concentration of 10 mM and a hydrochloric acid concentration of 1 mM.

IMS-MS coupled to infrared multiple photon dissociation (IRMPD)

spectroscopy. A home-built hybrid drift-tube quadrupole TOF mass spectrometer equipped with nanoelectrospray source was used for this work. The instrumental details are described elsewhere^{25,42–44}. A small aliquot (5–10 μ l) of sample solution was loaded on a Pd/Pt-coated borosilicate emitter and electrosprayed into the instrument. The spray voltage was set at -1.0 kV to generate negatively charged ions. Ions were collected in an ion funnel, pulsed into an 80-cm-long drift tube, and passed through helium buffer gas (4-5 mbar) under the influence of a weak electric field (10-15 V cm⁻¹). Ions were separated as a consequence of their drift velocities depending on their size and charge. At the end of the drift tube, a second ion funnel collected and transferred ions into the high-vacuum region. By varying the timing of a high-voltage pulse (-4.5 kV), which pulsed a fraction of ion mobility-separated ions into orthogonal TOF, a drift-time-selected TOF mass spectrum was recorded in the drift time range 5-14 ms. The arrival time distribution (ATD) was constructed by extracting the drift-time-dependent ion current of specific m/z ions. CCSs were determined using the measured drift time and the Mason-Schamp equation⁴⁵. To measure size- and conformer-selective infrared spectra, a narrow fraction of ions were selected by electrostatic deflection after ion mobility separation, and m/zselection was carried out in a quadrupole mass filter. The ion mobility- and m/z-selected ions were then irradiated by infrared photons from the Fritz Haber Institute free-electron laser (FHI FEL)⁴⁶. When the photon energy of the IR light was in resonance with an infrared active vibration of the ion, absorption of multiple photons and subsequent dissociation could occur. The abundances of precursor and fragment ions were recorded using the TOF mass analyser. Fragment TOF mass spectra obtained with low and high laser fluence are shown in Supplementary Fig. 4. IR spectra were obtained by scanning the laser in 3 cm⁻¹ steps in the range 1,000–1,900 cm⁻¹ and plotting the fragmentation efficiency as a function of wavenumber.

Calculation details. The initial geometry of the doubly-chlorinated homochiral serine octamer was generated and pre-optimized with the OPLS3 force field using MacroModel⁴⁷. The pre-optimized structure was further optimized using Gaussian09 (ref. 48) at the PBE0 level of density functional theory using the cc-pVTZ basis set and Grimme D3 dispersion corrections³⁹. Harmonic vibrational frequencies were calculated from the optimized structure, scaled by 0.957 (ref. 49) and convoluted with Gaussian functions of 10 cm⁻¹ bandwidth to construct the theoretical infrared spectrum. The theoretical CCS of the optimized structure was calculated using the trajectory method⁵⁰. For the energetics, counterpoise calculations were performed to estimate the effect of basis set superposition error (Supplementary Table 4).

Data availability. The data that support the findings of this study are available from the authors upon reasonable request.

Received 22 November 2016; accepted 6 June 2017; published online 10 July 2017

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Acknowledgements

The authors acknowledge the expert assistance of the FHI free electron laser facility staff, in particular S. Gewinner and W. Schöllkopf. M.T.B. acknowledges the Alexander von Humboldt Foundation and the National Science Foundation (USA) for support under grants CHE-1301032 and CHE-1565941.

Author contributions

J.S., S.W., K.P., M.T.B. and G.v.H. conceived and designed the experiments. J.S. and S.W. performed the experiments. J.S. analysed the data and suggested the structure of the serine octamer with two chlorides. All authors co-wrote the paper.

Additional information

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Competing financial interests

The authors declare no competing financial interests.