

Aqueous Sulfate Separation by Crystallization of Sulfate–Water Clusters

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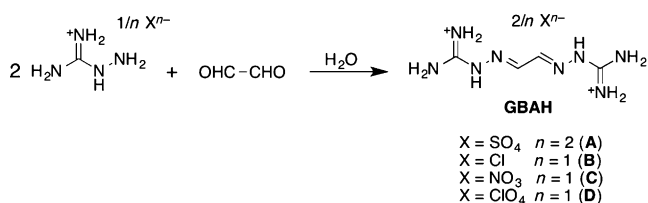
Abstract: An effective approach to sulfate separation from aqueous solutions is based on the crystallization of extended $[\text{SO}_4(\text{H}_2\text{O})_5]^{2-}$ sulfate–water clusters with a bis(guanidinium) ligand. The ligand was generated *in situ* by hydrazone condensation in water, thereby bypassing the need for elaborate syntheses, tedious purifications, and organic solvents. Crystallization of sulfate–water clusters represents an alternative approach to the now established sulfate separation strategies that involve encapsulation of the “naked” anion.

With a free energy of hydration of $-1080 \text{ kJ mol}^{-1}$,^[1] sulfate is one of the most hydrophilic anions found in nature. The extreme water affinity of sulfate originates from its high charge density and its ability to accept multiple hydrogen bonds from water. Theoretical and experimental studies have demonstrated the existence of a variety of $\text{SO}_4(\text{H}_2\text{O})_n^{2-}$ sulfate–water clusters in the gas, liquid, or crystalline state, and indicated that it takes twelve water molecules to complete the first hydration sphere of sulfate.^[2]

As a result of its strongly hydrated structure, sulfate is difficult to separate effectively and selectively from aqueous solutions, especially from mixtures containing less hydrophilic anions, such as nitrate or perchlorate.^[3] Although a number of sulfate-binding receptors have been reported,^[4] to date, only a small fraction of them have been demonstrated to separate sulfate efficiently from water by either solvent extraction^[5] or crystallization.^[6] By analogy with natural anion receptors, such as the sulfate-binding protein, it had generally been assumed that for strongly hydrophilic anions (e.g., sulfate, phosphate, selenate, chromate), effective aqueous binding and separation from water requires tight encapsulation of the anion within rigid, complementary host structures that completely sequester the anion from the water solvent.^[7] Whereas these principles remain valid and will continue to guide the design of anion receptors, we herein report an alternative approach to sulfate separation from water, where extended $[\text{SO}_4(\text{H}_2\text{O})_5]^{2-}$ sulfate–water clusters are selec-

tively crystallized with a bis(aminoguanidiniumhydrazone) cation self-assembled *in situ* from water-soluble subcomponents. This study demonstrates that at least in the case of crystallization, separation of the anion as a water cluster offers a viable alternative to the now established approach involving encapsulation of the “naked” anion.

Condensation of different aminoguanidinium salts with glyoxal in water yielded glyoxal bis(aminoguanidiniumhydrazone) (GBAH) as the sulfate (**A**), chloride (**B**), nitrate (**C**), or perchlorate (**D**) salt (Scheme 1).



Scheme 1. Preparation of the GBAH salts **A** to **D** by hydrazone condensation in water.

GBAH salts were first reported by Dralle and Thiele in 1898,^[8] and more recently, they were studied as antileukemic agents.^[9] These compounds caught our attention as potential anion separation agents because of the guanidinium groups contained in their structures. Guanidines are well-known oxoanion-binding groups,^[10] which prompted us to explore their potential for oxoanion separation by selective crystallization, an approach that proved so productive with the structurally related urea groups.^[6] We expected that the positive charge on the guanidinium groups would provide enhanced anion-binding strength through charge-assisted hydrogen bonding and improved water solubility compared to urea analogues. In the case of GBAH, we found the prospect of aqueous *in situ* self-assembly by hydrazone condensation particularly appealing, which could completely eliminate the need for extensive ligand synthesis and the utilization of organic solvents, which render so many traditional anion receptors impractical for real-world applications.

Mixing aqueous solutions of aminoguanidinium sulfate and glyoxal led to *in situ* formation of the GBAH cation and its crystallization as the sulfate salt **A**. Single-crystal X-ray diffraction analysis^[11] revealed that **A** crystallized with five water molecules (Figure 1 a). Hydrogen bonding between the water molecules and the sulfate anion led to the formation of one-dimensional $[\text{SO}_4(\text{H}_2\text{O})_5]^{2-}$ clusters running along the crystallographic *b* axis (Figure 1 b). Each sulfate in the cluster accepts eight hydrogen bonds from neighboring water molecules, with O–H···O contact distances ranging from 1.89 to

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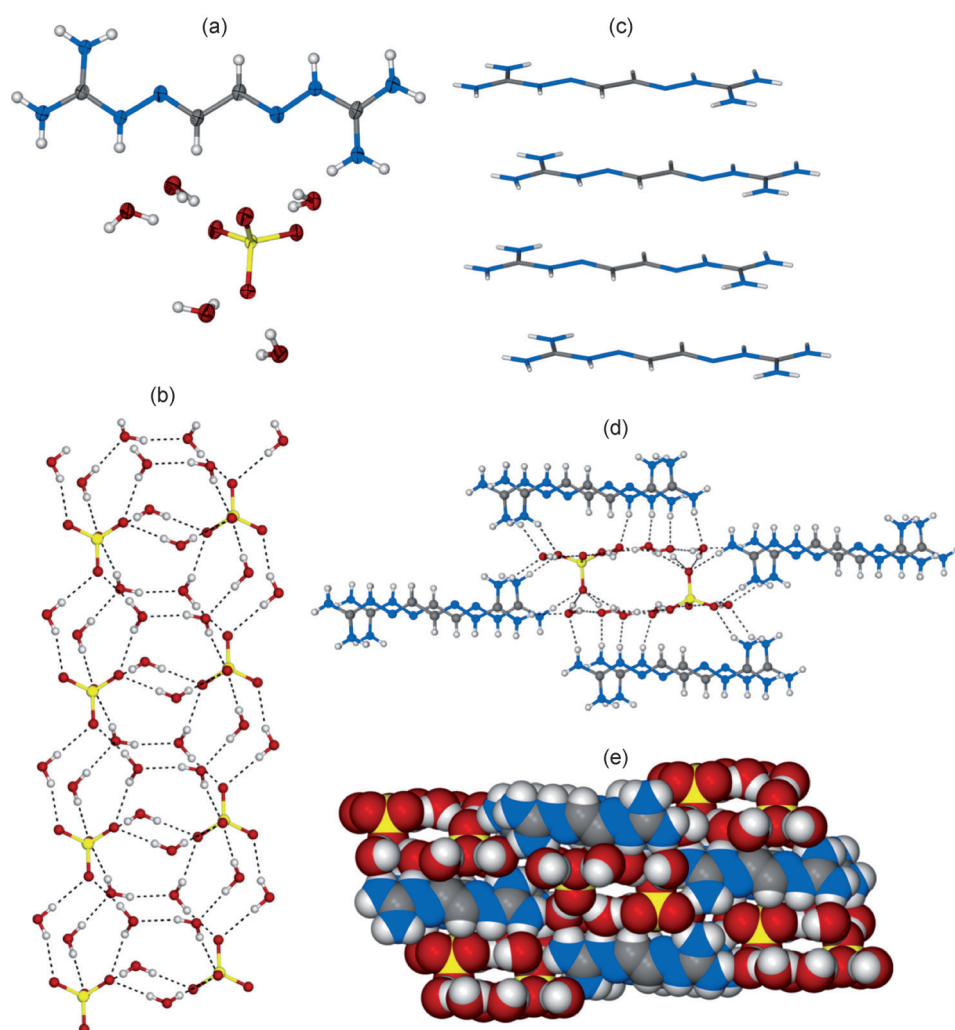


Figure 1. X-ray crystal structure of **A**. a) ORTEP representation showing the GBAH cation and the anionic $\text{SO}_4(\text{H}_2\text{O})_5^{2-}$ cluster. b) Hydrogen-bonded $[\text{SO}_4(\text{H}_2\text{O})_5^{2-}]_n$ clusters. c) Stacking of the GBAH cations. d) Hydrogen bonding of the sulfate–water clusters by the cationic GBAH stacks, viewed down the crystallographic b axis. e) Space-filling representation of the crystal packing viewed down the crystallographic b axis.

2.14 Å and O–H–O angles between 133.8 and 176.2°. Thus, sulfate retained two thirds of its hydrogen bonding upon crystallization, considering that on average, this anion accepts twelve hydrogen bonds from the first hydration sphere in the aqueous state.^[2] Additional hydrogen bonding between water molecules completes the cluster network, which comprises three types of sulfate–water ring topologies, with $R_5^3(10)$, $R_4^4(12)$, and $R_6^5(14)$ graph set notations. The clusters have an ellipsoid-shaped cross-section measuring approximately 10.5 Å between the two outmost points.

The GBAH cations adopt a virtually planar conformation in the crystal and stack along the crystallographic b axis with mean interplanar distances alternating between 3.10 and 3.20 Å (Figure 1c). Adjacent cations within each stack are slightly offset relative to each other, thereby creating arrays of four N–H hydrogen-bond donors spaced approximately 3.5–3.7 Å apart, each donating a hydrogen bond to a different water molecule in the cluster (Figure 1d). The fifth water molecule is isolated from the rest of the cluster and accepts an

N–H hydrogen bond from the other end of the cationic stack. The peripheral water molecules in the cluster also accept an additional hydrogen bond from neighboring stacks, and each sulfate anion accepts three N–H···O hydrogen bonds from two guanidinium groups in adjacent stacks. Therefore, it appears that the observed structure of the sulfate–water cluster is determined to a large extent by the geometry of the GBAH cation and its stacking in the crystal. The overall crystal packing, consisting of alternating cationic stacks and anionic sulfate–water clusters, is illustrated in Figure 1e.

Reaction of aminoguanidinium nitrate or perchlorate with glyoxal in water led to crystallization of the corresponding GBAH salts **C** and **D**. Single-crystal X-ray diffraction analysis^[11] showed that both salts crystallized in layered structures held together by anion–guanidinium hydrogen bonding (Figure 2). In the nitrate structure, the layers are almost perfectly flat and stacked on top of each other, whereas in the perchlorate structure, the layers are corrugated and interlinked by additional N–H···O hydrogen bonds between the guanidinium and the perchlorate ions.

The chloride salt **B** could also be synthesized in situ from aqueous aminoguanidinium chloride and glyoxal. However, no crystallization was observed under these conditions owing to the much higher aqueous solubility of this salt.^[12]

During the initial crystallization experiments, it became apparent that all of the oxoanions studied formed relatively insoluble salts with the GBAH cation, which prompted us to investigate the possibility for selective oxoanion separation by crystallization of these simple bis(guanidinium) salts. Table 1 lists the measured aqueous solubilities of **A** to **D** at 25°C, which follow the order $\mathbf{B} \gg \mathbf{D} > \mathbf{C} > \mathbf{A}$. Thus sulfate salt **A** has the lowest aqueous solubility in the series, in spite of the much higher free energy of hydration of SO_4^{2-} compared to the other anions.^[1] The corresponding solubility product constant (K_{sp}) for **A** is $3.2(5) \times 10^{-7}$, which is comparable to that of SrSO_4 ($K_{\text{sp}} = 3.4 \times 10^{-7}$), one of the least soluble inorganic sulfate salts. For comparison, the aqueous solubilities of plain guanidinium salts are much higher, and follow the order sulfate > chloride \gg nitrate > perchlorate,^[13] which essentially

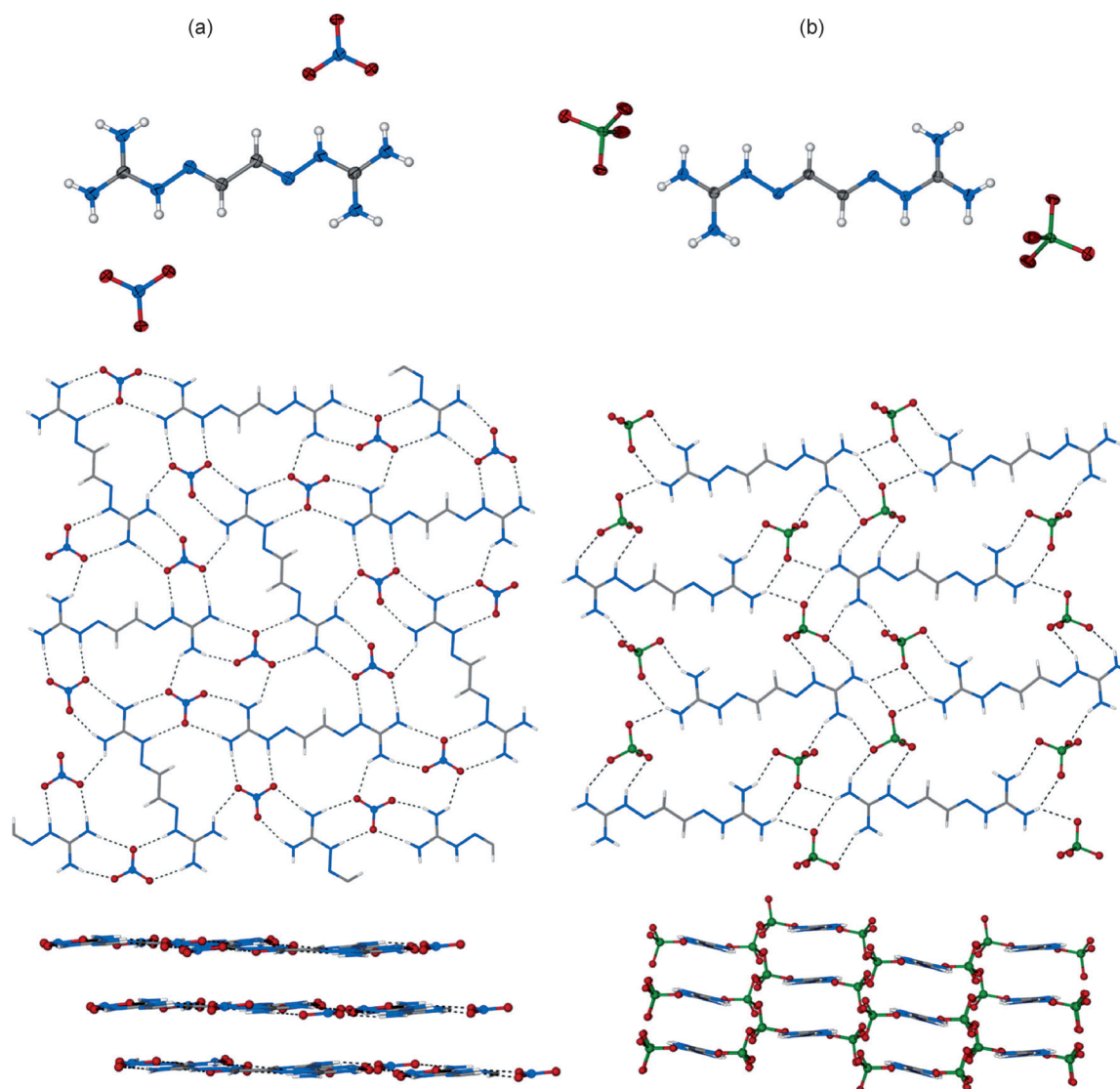


Figure 2. X-ray crystal structures of **C** (a) and **D** (b). Top: ORTEP representations; middle: hydrogen-bonded layers; bottom: packing of the layers.

Table 1: Aqueous solubilities of **A** to **D** at 25 °C.

Compound (anion)	Solubility [M]
A (SO_4^{2-}) ^[a]	$7.2(6) \times 10^{-4}$
B (Cl^-) ^[b]	0.88(8)
C (NO_3^-) ^[a]	$1.2(2) \times 10^{-3}$
D (ClO_4^-) ^[a]	$1.36(1) \times 10^{-2}$

[a] Measured by UV spectroscopy. [b] Determined gravimetrically.

reflects the order of the free energies of hydration of the anions (Hofmeister bias).

The observed solubility trend in the **A** to **D** series suggested that this simple bis(guanidine) system might prove effective in aqueous sulfate separation by selective crystallization of **A**. To test this hypothesis, we performed a series of competitive crystallization experiments consisting of the in situ synthesis of the GBAH cation (according to Scheme 1) in aqueous solution in the presence of various

anion mixtures (Table 2). The identity of the resulting crystalline product was confirmed by powder X-ray diffraction (PXRD) and Fourier-transformed infrared spectroscopy (FTIR) for each experiment. None of the starting amino-guanidinium salts can crystallize under these conditions owing to their much higher solubilities (3.0 to 3.7 M)^[14] compared to the GBAH salts. An equimolar aqueous mixture of sulfate (0.25 M) and perchlorate (0.25 M), which are the most and the least hydrophilic anions in the series, led to exclusive crystallization of **A** in 89% yield (Table 2, entry 1), resulting in a reduction of the sulfate concentration in solution to 0.0275 M. Similarly, **A** crystallized exclusively from a mixture of sulfate (0.25 M) and chloride (0.25 M), with a maximum observed yield of 93%, corresponding to a final sulfate concentration of 0.02 M (entry 2). On the other hand, a crystalline mixture of **A** and **C** was isolated from the competition experiment between sulfate and nitrate (entry 3), whereas **C** crystallized exclusively from a mixture of nitrate and perchlorate (entry 4). Thus the anion selectivities from these

Table 2: Competitive crystallization experiments.^[a]

Entry	Anion mixture (M)	Crystalline product
1	SO ₄ ²⁻ (0.25), ClO ₄ ⁻ (0.25)	A
2	SO ₄ ²⁻ (0.25), Cl ⁻ (0.25)	A
3	SO ₄ ²⁻ (0.25), NO ₃ ⁻ (0.25)	A (26%) and C (74%) ^[b]
4	NO ₃ ⁻ (0.25), ClO ₄ ⁻ (0.25)	C
5	SO ₄ ²⁻ (0.07), Cl ⁻ (0.07), NO ₃ ⁻ (0.07), ClO ₄ ⁻ (0.1)	A (24%) and C (76%) ^[b]

[a] All crystallizations were done in deionized water at room temperature.

[b] Molar composition determined gravimetrically by dissolution of the crystals with 1 M HCl and sulfate precipitation with BaCl₂.

pairwise competitive crystallizations are generally consistent with the measured solubilities of **A** to **D**. Finally, a competitive crystallization experiment with an aqueous mixture containing all four anions (entry 5) led once more to co-precipitation of **A** and **C**, the two least soluble compounds of the series.

The demonstrated anion selectivity in the crystallization of the GBAH salts is remarkable for such a simple bis(guanidinium) ligand. The observed selectivity for sulfate and nitrate stands in direct contrast with the anion selectivity in competitive crystallization of plain guanidinium salts, which favored the least hydrophilic perchlorate anion, in agreement with the Hofmeister bias.^[13] Unlike previously reported ligands used for sulfate crystallizations,^[6,15] which require cumbersome syntheses and purifications involving toxic reagents and solvents, the GBAH ligand can be generated in situ in pure water from simple subcomponents, which makes for a more practical, cheaper, and greener anion-separation method. Furthermore, as the GBAH ligand was generated by hydrazone condensation, a reversible bond-forming reaction commonly employed in dynamic combinatorial chemistry (DCC),^[16] it may be expected that even less soluble and more selective sulfate crystallization systems could be identified by DCC. Meanwhile, the current system may already find practical applications related to sulfate or/and nitrate separation. For example, both sulfate and nitrate can pose environmental problems as they are the main constituents of acid rain and can contaminate the groundwater.^[17] The presence of sulfate in seawater presents challenges for oil field injection operations because of scale formation.^[18] Sulfate is also a problematic constituent of legacy nuclear wastes,^[3] which could be targeted for sulfate separation alongside the more abundant nitrate. We envision that this crystallization approach could be applied to either the individual separation of sulfate or nitrate or a mixture of the two anions, depending on the practical need and the solution composition.

From a fundamental perspective, the present system demonstrates a new paradigm in sulfate separation, wherein the anion is crystallized as a sulfate–water cluster. This strategy presents some potential advantages over the traditional approach based on sequestration of the “naked” anion, such as a lower thermodynamic penalty associated with anion dehydration and enhanced selectivity based on exclusive recognition patterns associated with the unique structure of the cluster. In the case in point, sulfate crystallization as [SO₄(H₂O)₅]²⁻ clusters proved far more effective and selec-

tive than crystallization of plain guanidinium sulfate, even though in the latter case, the sulfate is completely dehydrated and coordinatively saturated by twelve NH hydrogen bonds.^[19] We attribute the much lower solubility of **A** compared to plain guanidinium sulfate to mainly two factors: an energetically favorable stacking of the GBAH cations and a lower dehydration penalty for sulfate, as the anion retains two thirds of the water hydrogen bonds from its first hydration sphere in crystalline **A**. On the other hand, the sulfate selectivity could be rationalized based on the specific recognition of the [SO₄(H₂O)₅]²⁻ clusters by hydrogen bonding from the GBAH stacks. Whereas this structure was discovered serendipitously, it could inspire the rational design of future sulfate crystallization systems based on the recognition of other sulfate–water clusters.

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