

Communication

Self-assembly architecture of bis(guanidiniums) receptors incorporated by sulfate anions in single crystals

LU, Guo-Yuan* (陆国元) SONG, Wei (宋伟) TANG, Feng (唐峰) JIN, Chuan-Min (金传明)
LIU, Fang (刘芳) WAN, Xiao-Bin (万小宾)

Department of Chemistry, Nanjing University, Nanjing, Jiangsu 210093, China

A novel bis(guanidiniums) receptor for the catalytic cleavage of phosphodiester was prepared and self-assembly architecture through hydrogen bonds and electrostatic interactions among the bis(guanidiniums) receptor, the sulfate anion and water molecule was revealed by X-ray crystallographic analysis.

Keywords Bis(guanidiniums), receptor, sulfate anion, hydrogen bond, self-assembly

Molecular self-assembly is ubiquitous in biological systems and underlies the formation of a wide variety of complex biological structures. The application of natural self-assembly phenomena to artificial systems has led to the concept of supramolecular self-assembly¹ and achieved a variety of novel supramolecular self-assembly aggregates such as double helices, rods, girds, tubes, cages, catenanes and interlocked systems.² In the supramolecular self-assembly systems, hydrogen bonds³ or metal cation coordinate bonds⁴ were very frequently recognized as intermolecular weak bonds. However, the self-assembly systems incorporated by the anions have so far received comparatively little attention.

The guanidinium group is a component of the arginine residue in proteins, which has an important function in biological systems. The guanidinium group remains protonated over a much wider range of pH than the ammonium group due to its much higher p*K* (13.5) value.⁵ Therefore, guanidinium derivatives have been successfully employed for the molecular recognition of the

anions, such as carboxylate (amino acids),^{6,7} phosphate (nucleotides)^{8,9} and sulfate^{10,11} *via* hydrogen bonding and electrostatic interactions. Especially, a number of bis(guanidiniums) receptors have been synthesized and used to mimic the enzyme staphylococcal nuclease (SN) in the past decade.¹² However, the crystal structures of bis(guanidiniums) receptors have not been reported so far.

Recently, we prepared¹³ a novel bis(guanidiniums) receptor from the reaction of *S*-methylisothiourea sulfate with 4-methyl 1, 3-bis(aminomethyl) phenol dihydrochloride (Scheme 1) which was available from 4-methyl phenol through a 3 step reaction.¹⁴ Compound 1: m.p. 308—309 °C. NMR, IR and elemental analysis data of compound 1 are in accord with the assigned structure.¹⁵ The dichloride salt of the bis(guanidiniums) receptor was also obtained by means of adding barium chloride to the dilute solution of 1 and removing the precipitated barium sulfate. The primary experiment also showed that the dichloride salt of the bis(guanidiniums) receptor is suitable for the catalytic cleavage of phosphodiester (bis(4-nitrophenyl) phosphate, as a simple model of DNA and RNA) in the solution of water-acetonitrile, which caused the increase of the reaction rate by about 300-fold. Evaporating the dilute aqueous solution of the pure 1 gave orange single crystals which were subject to X-ray crystallographic structure analysis.¹⁶

ORTEP view of compound 1 with one water molecule is given in Fig. 1. Selected bond lengths and bond angles are summarized in Table 1. In the two

* E-mail: nj.lgy@jlonline.com

Received March 30, 2000; accepted July 14, 2000.

Project supported by the National Science Foundation of China (No. 29872014).

guanidinium groups, the nearly equivalent C—N bond lengths indicate that the electron density is essentially delocalized. The average C—N length is 0.1343 nm and the average N—C—N bond angle is 120° , which are close to the theoretical values.¹⁷ In the crystal, the two guanidinium group planes make a dihedral angle of 87.9° and the dihedral angles between the guanidinium group and phenyl ring plane are 90.3° and 92.1° , respectively. Therefore these three planes are perpendicular to each other. The conformation of the receptor molecule is stabilized by an intramolecular hydrogen bond between the oxygen atom O(1) of the phenol group and N(2)—H ($N(2)\cdots O(1)$, 0.3143 nm, $N(2)-H\cdots O(1)$, 159.8°) as well as intermolecular hydrogen bond and electrostatic interactions.

Hydrogen bonding interactions provide the major driving force for self-assembly. In the crystal, sulfate anions and water molecules are connected with each other to form the chains along *b* axis by hydrogen bonds (Fig. 2). For each water molecule, besides the two hydrogen bonds with sulfate anion, the two lone electron pairs of oxygen atom O(6) form two additional hydrogen bonds with the guanidinium group and phenol hydroxy group respectively ($O(6)\cdots N(2)$, 0.3011 nm; $O(6)\cdots H-N(2)$, 153.5° ; $O(6)\cdots O(1)$, 0.2856 nm; $O(6)\cdots H-O(1)$, 155.3°). Therefore, the water molecules form tetrahedral hydrogen bonding network just as they do in ice. For sulfate anion, besides two hydrogen bonds with water, eight others are formed between the oxygen atoms and N—H of the guanidinium groups and so all N—H of guanidinium groups are involved in the hydrogen bonds with the oxygen atoms of water molecule, sulfate anion or phenol group respectively (Table 2). Therefore, the whole hydrogen bonding network is formed *via* the sulfate-water chains (Fig. 3) due to the tetrahedral structure of the sulfate oxoanions.

Electrostatic interactions also play a role in self-assembly. Positively-charged guanidinium cations are situated in proximity to negatively-charged sulfate oxoanions (Fig. 3). It is also notable that the *p*-methyl phenol rings are in *anti*-parallel arrangement along the *a* axis. The distance between the adjacent aromatic rings is 0.336 nm which falls within the distance range of π - π stacking interaction.¹⁸ Therefore, arene-arene stacking interaction is also an important non-covalent force in this self-assembly.

Scheme 1 Synthesis of the bis(guanidiniums) receptor

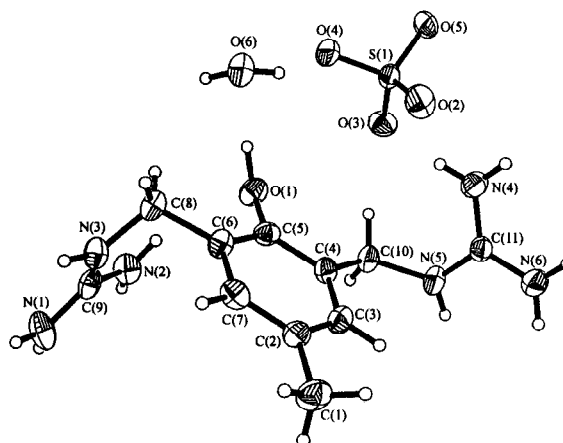
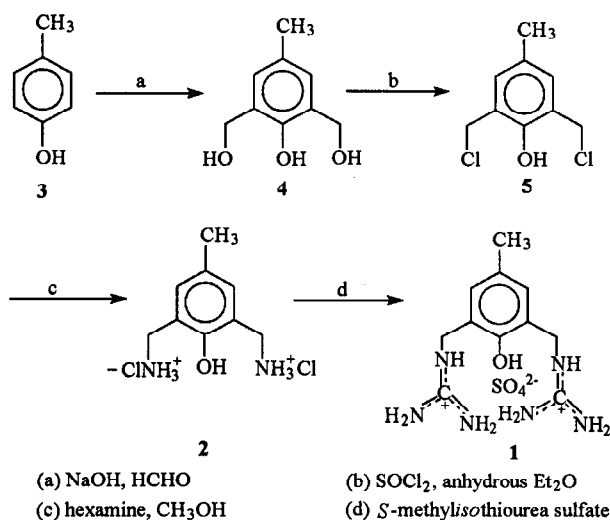


Fig. 1 ORTEP view of the compound 1 including one water molecule with the atomic numbering system.

Table 1 Selected bond lengths (nm) and bond angles($^\circ$)

S(1)—O(2) 0.1460(2)	O(2)—S(1)—O(4) 110.3(1)
S(1)—O(4) 0.1484(2)	O(2)—S(1)—O(3) 110.7(1)
S(1)—O(3) 0.1494(2)	O(4)—S(1)—O(3) 108.3(1)
S(1)—O(5) 0.1505(2)	O(2)—S(1)—O(5) 109.2(1)
	O(4)—S(1)—O(5) 108.3(1)
	O(3)—S(1)—O(5) 110.0(1)
N(1)—C(9) 0.1353(4)	N(2)—C(9)—N(3) 122.0(3)
N(2)—C(9) 0.1327(4)	N(2)—C(9)—N(1) 118.9(3)
N(3)—C(9) 0.1343(4)	N(3)—C(9)—N(1) 119.2(3)
N(4)—C(11) 0.1350(3)	N(6)—C(11)—N(4) 120.8(2)
N(5)—C(11) 0.1364(4)	N(6)—C(11)—N(5) 118.2(2)
N(6)—C(11) 0.1325(3)	N(4)—C(11)—N(5) 121.0(2)

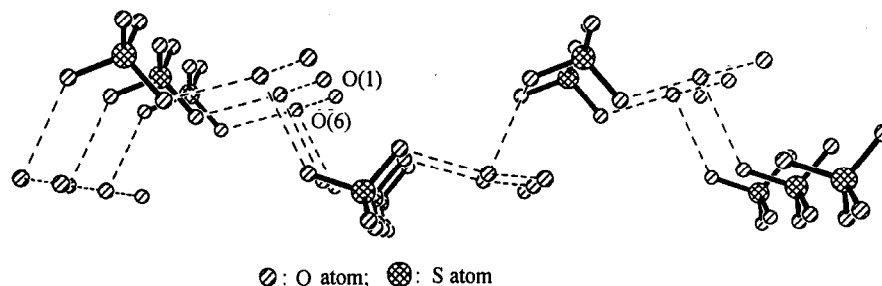


Fig. 2 A chain of sulfate oxoanions *via* water molecules and the oxygen atoms O(1) of phenol group. Hydrogen atoms are omitted for clarity.

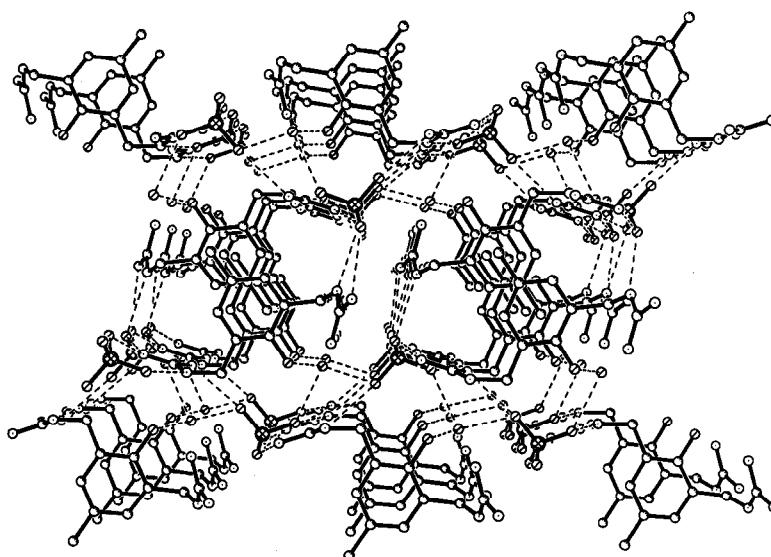


Fig. 3 Packing diagram viewed from the *a* axis (Hydrogen atoms are omitted for clarity).

Table 2 Hydrogen bonds for the guanidinium groups

D—H...A	d(D...A) (nm)	∠D—H...A(°)
N(1)—H...O(5) # 1	0.3017	142.1
N(1)—H...O(5) # 2	0.2929	166.9
N(2)—H...O(1) # 3	0.3143	159.8
N(2)—H...O(6) # 4	0.3011	153.5
N(3)—H...O(3) # 2	0.2897	171.8
N(4)—H...O(4) # 5	0.3052	160.0
N(4)—H...O(2) # 3	0.2909	140.6
N(5)—H...O(4) # 6	0.2917	156.1
N(6)—H...O(3) # 5	0.2897	168.0
N(6)—H...O(5) # 6	0.2938	161.0

Symmetry operators: # 1, $x + 1, -y + 1/2, z - 1/2$; # 2, $-x + 1, y - 1/2, -z + 1/2$; # 3, x, y, z ; # 4, $x + 1, y, z$; # 5, $x, -y + 1/2, z + 1/2$; # 6, $x + 1, -y + 1/2, z + 1/2$.

In conclusion, the bis(guanidinium) receptors are spontaneously self-assembled along the sulfate anion-water chains. The driving forces come from the formation of hydrogen bonding network, electrostatic interactions be-

tween guanidinium cations and sulfate anions as well as arene-arene stacking interaction.

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15. ν_{\max} : 3300, 3150(N—H), 1660(C=N) cm^{-1} . $\delta_{\text{H}}(\text{D}_2\text{O})$: 7.28(s, 2H, ArH), 4.52(s, 4H, $2 \times \text{ArCH}_2\text{N}$), 2.30(s, 3H, ArCH₃). Anal. C₁₁H₂₀N₆O₅S. Calcd: C, 37.92; H, 5.79; N, 24.12. Found: C, 37.84; H, 5.93; N, 24.34.
16. Crystal data for C₁₁H₂₂N₆O₅S (including 1H₂O): $M = 366.41$, monoclinic, space group: $P2_1/c$ $a = 0.76433(15)$, $b = 1.9447(4)$, $c = 1.2115(2)$ nm, $\beta = 107.81(3)^\circ$, $U = 1.7145(6)$ nm³, $T = 293(2)$ K, $Z = 4$, $d_{\text{calc}} = 1.420$ g/cm³, $\mu = 0.230$ mm⁻¹, Reflections collected/unique 2654/2654 [$R_{\text{int}} = 0.000$], Final R indices [$I > 2\sigma(I)$], $R = 0.0654$, $wR = 0.1605$. A single crystal having dimensions of 0.30 × 0.30 × 0.20 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS-IV imaging plate area detector with graphite monochromated Mo K_α radiation. The structure was solved with direct method and refined by full-matrix least-squares method on F^2 .
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(E200003074 SONG, J.P.; LING, J.)