HALOGEN AND HYDROGEN HOST-GUEST BONDING IN CLATHRATE HYDRATES

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ABSTRACT
Clathrate hydrates with low melting points (often below –20°C) are difficult subjects for single crystal data collection. A high level of guest molecule disorder inside the high symmetry cages causes difficulty for structure determination of such crystals as well. Recent advances in single crystal X-ray diffraction have allowed this technique to be used as a valuable tool for the analysis of hydrate structure and composition. With detailed analysis of guest and water molecules disorder, not only the guest positions are clearly defined, but also it becomes possible to find interactions between guest and water molecules.

For the first time, single crystal x-ray crystallography is used to detect the presence of guest host hydrogen and halogen bonding in structure I, II and structure H clathrate hydrates. Clathrates studied are the tert-butylamine (tBA) sII clathrate with H₂S and Xe help gases, the pinacolone + H₂S binary sH clathrate, 1,3-Dioxolane hydrate, chlorine, bromine, and mixed chlorine with bromine hydrates.

X-ray structural analysis shows that the tBA nitrogen atom has a distance of 2.64 Å from the closest large cage oxygen atom. This water molecule is pulled inwards toward the tBA guest (cage center) and the structure of the large cage is substantially distorted in comparison to the ideal cage structure. The pinacolone oxygen atom is determined to have a distance of 2.96 Å from the closest large cage oxygen atom.

Keywords: clathrate hydrates, crystal structure, chlorine, bromine, pinacolone, tert-butylamine.

INTRODUCTION
Clathrate hydrates are traditionally considered to form when a hydrophobic molecules or molecules with large hydrophobic moieties are pressurized with water or ice at low temperatures.[1] The molecular driving force of the hydrate formation is considered to be minimization of the water-hydrophobic interactions by forming water cages that isolate the guests by encapsulation. However, it has long been known that this picture is not complete and guest molecules misible in water also form clathrates if compressed under proper thermodynamic conditions. These water-miscible guest molecules have hydrophilic functional groups in addition to the hydrophobic moieties of the molecule and have been predicted to form hydrogen bonds with the water molecules in the solid clathrate structures. Recent evidence from direct single crystal X-ray crystallographic observation of the hydrogen bonding in the hydrate structure in the sH pinacole and sII tert-butylamine binary hydrates. [2] differences between NMR relaxation times [3] and pressure – temperature phase boundaries [4] of similarly structured guest molecules with and without hydrogen bonding functional groups, IR vibrational frequencies [5], and observations from molecular dynamics simulations [2-6] shown

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direct evidence of hydrogen bonding of guest molecules with hydrophilic functional groups.

In this paper, we show the results of single crystal X-ray structural analysis of hydrogen bonding in the structure II clathrate hydrate phases of the water miscible tert-butylamine with H₂S and Xe help gases, and 1,3-Dioxolane, in structure H clathrate of the water miscible pinacolone with H₂S. We will show halogen host-guest interactions in structure I chlorine hydrate, mixed structure I chlorine and bromine hydrate, and tetragonal structure bromine hydrate. Understanding gained from studying factors that affect formation of clathrate hydrates with water miscible guests can help in the design of better hydrate formation inhibitors and lead to the design of other hydrate structures with polar and water soluble guests species.

SYNTHESIS, X-RAY COLLECTION, AND STRUCTURE SOLUTIONS

The samples of pinacolone + H₂S clathrate strH and tert-butylamine (tBA) sII clathrate with H₂S and Xe were prepared by placing powdered ice and the liquid guest in Pyrex tubes, ice being in slight excess. Each Pyrex tube was connected to a vacuum line with a ground glass joint. After cooling of the end of the Pyrex tube that contained the powdered ice and liquid guest in liquid nitrogen, air was removed under dynamic vacuum and a measured volume of the gas (sufficient to fill all of the small cages in the hydrate structures) was condensed on top of the frozen mixture. The tube was then flame-sealed, the cold mixture meanwhile being kept in liquid nitrogen. After sealing, the sample was allowed to warm slowly to -40°C in a freezer. Single crystals of sufficient quality for X-ray diffraction grew slowly during storage over several years.

Single crystals of chlorine, and mixed chlorine with bromine hydrates were grown in a sealed tubes from 1:4 chlorine to water and 1:1:8 chlorine to bromine to water solutions at -40 °C over a period of several months.

Single crystals of bromine hydrate were grown in a tubes from 1:6 bromine to water solutions at -5 °C over a period of several months.

Single crystals of 1,3-Dioxolane hydrate were grown in a tubes from 1:14 1,3-Dioxolane to water solutions at -40 °C over a period of several months.

Crystals suitable for diffraction were selected using a microscope mounted in a cold box. Subsequent handling and transfer of the crystals were always done under cold conditions where the crystals were stable.

Single crystal X-ray diffraction data were measured on a Bruker Apex 2 Kappa diffractometer at 100 K, using graphite monochromatized Mo Kα radiation (λ = 0.71073 Å). The unit cell was determined from randomly selected reflections obtained using the Bruker Apex2 automatic search, center, index, and least squares routines. Integration was carried out using the program SAINT, and an absorption correction was performed using SADABS. [7] The crystal structures were solved by direct methods and the structure was refined by full-matrix least-squares routines using the SHELXTL program suite. [8] All atoms were refined anisotropically. Hydrogen atoms on guest molecules were placed in calculated positions and allowed to ride on the parent atoms.

RESULTS AND DISCUSSION

tert-Butylamine + (H₂S, Xe) sII clathrate: Pure tBA forms a structure VI clathrate hydrate upon compression with water (1:10 tBA to water ratio).[9–11] (Fig.1) In more concentrated solutions (1:7 tBA to water) tBA forms a semiclathrate of orthorhombic structure (Fig.2). Nitrogen atom of tBA in this structure replaces the...
water molecule from a water framework and forms a strong hydrogen bond with another water molecule. (Fig.3). In the presence of helper gases (a mixture of H₂S and Xe in the present case), tBA forms a sII clathrate hydrate [11-13]. The single-crystal X-ray structure of the binary tBA + H₂S/Xe sII hydrate gives the placement of the tBA molecule in the large sII cage as shown in Figure 4. The experimentally measured N–OW distance is determined as 2.64 Å. The experimentally determined structure shows that the water molecule hydrogen-bonded to the amine nitrogen has been displaced by about 1 Å towards the centre of the cage.

**Fig.2.** Orthorhombic t-Butylamine •7.25H₂O hydrate (view along b axis).

**Fig.3.** Orthorhombic t-Butylamine •7.25H₂O hydrate.

**Fig.4.** t-Butylamine in large cage of structure II hydrate.

**Pinacolone + H₂S sH clathrate:** (Fig.5) The X-ray structure of pinacolone in the large sH cage, viewed looking parallel to the C6 axis (polar axis)

**Fig.5.** Pinacolone and H₂S molecules in structure H hydrate cages.
of the cage at 100 K, is shown in Figure 6. The long axis of the molecule is oriented in the polar direction of the cage. The carbonyl oxygen of pinacolone is positioned at a distance of 2.96 Å from a water molecule in the equatorial plane of the large sH cage. Although the water hydrogen atom is not visible in this structure, the pinacolone-O···H-O-H distance is consistent with hydrogen bonding between the pinacolone molecule and the cage water. The oxygen atom of the hydrogen-bonded water molecule is not appreciably pulled out of the “ideal” position in the cage towards the pinacolone guest.

**Bromine clathrate hydrate:** Bromine forms unique tetragonal hydrate structure. This structure was first studied in 1963 by K. W. Allen and G. A. Jeffrey [14]. We studied bromine structure in 1997 [15] but at that time we were not able to localize positions of bromine molecules in cages. In this paper we present results of structure refinement with exact molecules positions inside the cages. The bromine molecules are located in the large T- and P-cavities while the small dodecahedral cavities are vacant or partially occupied by O₂ or
N$_2$ molecules that are incorporated during crystallization in air. The bromine molecules are disordered in such a way that it is possible to determine 6 crystallographically independent sites in the T$_A$ cavity, 8 sites in the T$_B$ cavity, and 6 sites in the P cavity.

The locations of the molecule in the T$_A$ cavity are shown in Figure 7. It should be noted that there are no bromine sites along the axis going through the centers of the hexagonal sides of the cage. This might be due to the fact that the T$_A$ cavity is slightly compressed along this axis, which makes it impossible for the bromine molecule to be located there. Bromine molecules are arranged in a somewhat different way in the T$_A$ (Fig.7) and T$_B$ (Fig.8) cages although they have the same symmetry. This means that the bromine atoms have a different number of positions and a different distribution over these positions. So, two 14-hedral cavities, which have the same symmetry are crystallographically distinct and have different types of disorder for the encaged bromine molecules. Disordering of the bromine molecule in the P-cavity is illustrated in Figure 9. The minimum intermolecular Br-O distance due to halogen bonding in T$_B$ cage is 2.91Å, significantly less than sum of van-der vaals radii (3.37Å), indicating strong halogen interaction (Fig.10.). In small cage halogen interaction is even stronger and the shortest Cl-O distance is 2.90Å (Fig.11.).

**Fig.10. Chlorine molecule in structure I large cage.**

**Fig.11. Chlorine molecule in structure I small cage.**

**Chlorine and bromine clathrate hydrate:** Pure chlorine molecule forms halogen bonds with water framework. In large cage chlorine molecules are found close to plane parallel to hexagonal faces of the cage. The smallest Cl-O distance found is 3.07Å is much less than sum of van-der vaals radii (3.27Å), indicating strong halogen interaction (Fig.10.). In small cage halogen interaction is even stronger and the shortest Cl-O distance is 2.90Å (Fig.11.).

**Chlorine clathrate hydrate:** This structure was studied in 1952 by L. Pauling and R. Marsh [16].
bromine forms unique tetragonal hydrate structure, but in the 1:1 mixture with chlorine it forms cubic structure I and occupies large cages. Chlorine molecules are found in both small and large cages (Fig.12). Water framework in this structure is heavily disordered. All possible locations of water molecules in framework are shown in Figure 13. Both large and small cages are distorted and halogen interaction found for both bromine and chlorine molecules. Figure 14 shows one of the possible configurations of distorted small cages. Some of the cage edges are elongated from normal 2.7-2.8Å to 3.0 – 3.1Å.

The minimum intermolecular Cl-O distance in small cage is 2.80Å.

1,3-Dioxolane clathrate hydrate: The single-crystal X-ray structure of the 1,3-Dioxolane sII hydrate gives the placement of the 1,3-Dioxolane molecule in the large sII cage as shown in Figure 15. The experimentally measured O–O host-guest distance is determined as 2.74Å. The experimentally determined structure shows that the water molecule hydrogen-bonded to the guest oxygen has been displaced by about 0.56Å towards the center of the cage. The site occupancy of this water molecule depends on temperature of the experiment. We did several full data collections at different temperatures from 80 to 220 K. At 80 K this hydrogen bonded site is only 5% occupied and at 220 K it is 100 % occupied. Which means percentage of hydrogen bonded 1,3-dioxolane will vary from 5% to 100%, too (Fig.16).

CONCLUSIONS
Our investigation shows that in many cases water-miscible guest molecules with hydrophilic functional groups in addition to the hydrophobic moieties of the molecule form hydrogen bonds with the water molecules in the solid clathrate structures. Halogen molecules can form quite strong guest-host halogen bonds as well. In some cases host guest interactions needs displacement of water molecule from its original position.
Hydrogen bonding depends on the temperature of the experiment.

THE DETAILS OF THE X-RAY STRUCTURAL DETERMINATION

**tert-Butylamine (tBA) sII clathrate with H₂S and Xe help gases:** chemical formula C₄H₉NO₂S₈.₇₇Xe₂.₂₃, [0.23Xe·1.77(H₂S)·(C₄H₉)₄N·17H₂O], M = 470.93, Z = 8, crystal size 0.55×0.5×0.5 mm³, cubic space group Fd3m, a = 17.3983(2) Å, V = 5266.5(1)Å³, T = 100.0(1) K, ρ = 1.188 g/cm³, 53573 reflections measured, 1077 unique 633 [I>2σ(I)], final R indices [I>2σ(I)] R₁ = 0.0532, wR² = 0.1343, R indices (all data) R₁ = 0.1055, wR² = 0.134, largest differential peak and hole 0.78 and -0.57 e·Å⁻³, respectively.

**Pinacolone + H₂S binary sH clathrate:** chemical formula C₆H₉(NO₂S₈.₇₇S₈.₉₆, [4.96(H₄S)·C₆H₅·O·34H₂O], M = 881.72, Z = 1, crystal size 0.5×0.3×0.25 mm³, hexagonal space group P6/mmm, a = 12.159(1) Å, c = 10.026(2) Å, V = 1283.6(3)Å³, T = 100.0(1) K, ρ = 1.141 g/cm³, 16216 reflections measured, 772 unique 730 [I>2σ(I)], final R indices [I>2σ(I)] R₁ = 0.0116, wR² = 0.0307, R indices (all data) R₁ = 0.0319, largest differential peak and hole 0.20 and -0.15 e·Å⁻³, respectively.

**Bromine clathrate hydrate:** chemical formula Br₁.₈₂O₂·₄.₇₂[Br₂·9.1H₂O], M = 306.13, Z = 20, crystal size 0.4×0.3×0.3 mm³, tetragonal space group P4(2)/mmn, a = 23.044(1) Å, c = 12.075(1) Å, V = 6411.7(5) Å³, T = 173.0(1) K, ρ = 1.586 g/cm³, 24477 reflections measured, 2519 unique 1841 [I>2σ(I)], final R indices [I>2σ(I)] R₁ = 0.0484, wR² = 0.0853, R indices (all data) R₁ = 0.0747, largest differential peak and hole 0.66 and -0.27 e·Å⁻³, respectively.

**Chlorine clathrate hydrate:** chemical formula Cl₂.₀₂O₂·₇.₆₇Cl₂·7.₆₇H₂O, M = 209.02, Z = 8, crystal size 0.3×0.2×0.1 mm³, cubic space group Pm-3n, a = 11.9710(1) Å, V = 1715.50(2) Å³, T = 173.0(1) K, ρ = 1.619 g/cm³, 17919 reflections measured, 429 unique 360 [I>2σ(I)], final R indices [I>2σ(I)] R₁ = 0.1152, wR² = 0.0366, R indices (all data) R₁ = 0.0209, largest differential peak and hole 0.08 and -0.04 e·Å⁻³, respectively.

**Chlorine and bromine mixed clathrate hydrate:** chemical formula Cl₆.₃₃Br₆.₆₆O₆·₉₂, M = 352.42, Z = 8, crystal size 0.3×0.2×0.1 mm³, cubic space group Pm-3n, a = 11.9619(4) Å, V = 1711.6(1) Å³, T = 173.0(1) K, ρ = 1.710 g/cm³, 19633 reflections measured, 500 unique 384 [I>2σ(I)], final R indices [I>2σ(I)] R₁ = 0.0261, wR² = 0.0829, R indices (all data) R₁ = 0.0431, largest differential peak and hole 0.19 and -0.14 e·Å⁻³, respectively.

REFERENCES

