Hydrates of Organic Compounds. IV. Clathrate Hydrates of Various Bolaform Salts

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The solid-liquid phase diagrams are presented for binary mixtures of water with various polymethylenebis(tributylammonium) difluorides, $[(n\text{-}C_4H_9)_3N(CH_2)_nN(n\text{-}C_4H_9)_3]F_2$ (n=4, 5, 6, 8, and 10); and with hexamethylenebis(tributylammonium) dihydroxide and its salts, $[(n\text{-}C_4H_9)_3N(CH_2)_6N(n\text{-}C_4H_9)_3](X_2$ or Y) (X=OH, Cl, and Br; Y=OOC-COO and OOC-$(CH_2)_3$-COO). It has been found that all the compounds form congruently melting hydrates which have large hydration numbers. The hydrates appear to be clathrate-like hydrates essentially similar to those formed by many tetrabutyl(or isopentyl)ammonium salts. The most stable hydrate found in this study is $[(n\text{-}C_4H_9)_3N(CH_2)_6N(n\text{-}C_4H_9)_3]F_2$ hydrate (mp 20.4 °C). The melting points of hexamethylenebis(tributylammonium) hydrates have been compared with those of the corresponding tetrabutylammonium hydrates.

Bisquaternary ammonium salts (bolaform salts) having various hydrophobic groups have been studied from several points of view; the thermodynamic and transport properties *e.g.* molal volumes,[1-3] molal heat contents and solvation enthalpies,[4,5] heat capacities,[3,6] and conductances,[7,8] colloidal properties *e.g.* micelle formation,[9] flocculating action,[10] and emulsion polymerization,[11] pharmacological properties[12] *e.g.* protein binding,[13] resistance to metabolic degradation and accumulation in the kidneys,[14] affinity to choline and its related compounds,[15] and curarelike agent action.[16]

The thermodynamic and transport properties for aqueous solutions of bolaform salts as well as numerous symmetrical tetraalkylammonium salts[17] have extensively been studied in order to examine the structural changes in the solvent in the neighborhood of the solute particles. Broadwater and Evans[1] studied the apparent (ϕ_2) and partial molal volumes of a bolaform electrolyte $[(n\text{-}C_4H_9)_3N(CH_2)_8N(n\text{-}C_4H_9)_3]Br_2$ (C_8Br_2) and found the change of ϕ_2 with concentration for C_8Br_2 was very similar to that observed for $(n\text{-}C_4H_9)_4NBr$,[18] with ϕ_2 decreasing to a minimum and increasing with concentration. The minima in the ϕ_2 *vs.* concentration curves for $(n\text{-}C_4H_9)_4NBr$ have been correlated with the formation of a stable clathrate-like hydrate.[19-21]

In the same context it is of interest to examine the ability of bolaform salts to form clathrate-like hydrates. Although only a brief note has been given concerning the formation of C_8F_2 hydrate (which melts at 5 °C and has approximately 40 water molecules),[1] no other study has been reported about the formation of clathrate hydrates of bolaform salts. It is the purpose of this paper, through the examination of the solid-liquid phase diagrams, to find the conditions for the formation of clathrate-like hydrates of bolaform salts: (1) the length of methylene chain (n) between the two nitrogen atoms in the salt having the general formula $[(C_4H_9)_3N(CH_2)_nN(C_4H_9)_3]F_2$; and (2) the kind of anions in the salt $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]$ (X_2 or Y) (X=OH, F, Cl, and Br; Y=OOC-COO and OOC-$(CH_2)_3$-COO). The six alkyl chains attached to the two terminal nitrogen atoms have been restricted to butyl groups since it was concluded in a previous paper[22] that either the butyl or isopentyl chain was the most suitable size for the formation of stable clathrate hydrates of tetraalkylammonium fluorides.

The clathrate-like hydrates of bolaform salts may be regarded as extended hydrates which have large guest molecules rather than tetraalkylammonium salts, although tetraalkylammonium hydrates, in a sense, may be thought of as extended hydrates compared with ordinary gas hydrates.

Experimental

Polymethylenebis(tributylammonium) dibromides $[(C_4H_9)_3N(CH_2)_nN(C_4H_9)_3]Br_2$ (n=4, 5, 6, 8, and 10; which have been denoted as C_4Br_2, C_5Br_2, C_6Br_2, C_8Br_2, and $C_{10}Br_2$ hereafter) have been prepared by refluxing an excess of tributylamine with the corresponding α,ω-dibromoalkane in ethanol.[1] The excess amine was removed by extraction with diethyl ether and recrystallizations were carried out either in an acetone/ethyl acetate mixture or an diethyl ether/methanol mixture. Since it was fairly difficult to obtain pure $C_{10}Br_2$ by recrystallization, the C_{10}-compound was obtained as the iodide, $C_{10}I_2$, by the following procedure: $C_{10}I_2$ was precipitated by adding KI solution to aqueous $C_{10}Br_2$ solution which was then extract from the reaction mixture and recrystallized from ethyl acetate.

All the salts were confirmed by IR, NMR, and elemental analysis.

Found: C, 57.41; H, 10.69; N, 4.81; Br, 27.01%. Calcd for $C_{28}H_{62}N_2Br_2$ (n=4): C, 57.33; H, 10.65; N, 4.78; Br, 27.24%. Mp 157—158 °C for the bromide and 163—164 °C for the iodide.

Found: C, 58.02; H, 10.69; N, 4.62; Br, 26.90%. Calcd for $C_{29}H_{64}N_2Br_2$ (n=5): C, 57.99; H, 10.74; N, 4.66; Br, 26.61%. Mp 170—171 °C.

Found: C, 58.75; H, 10.99; N, 4.36; Br; 25.22%. Calcd for $C_{30}H_{66}N_2Br_2$ (n=6): C, 58.62; H, 10.82; N, 4.56; Br, 25.22%. Mp 167—168 °C.

Found: C, 59.60; H, 11.04; N, 4.27; Br, 25.32%. Calcd for $C_{32}H_{70}N_2Br_2$ (n=8): C, 59.80; H, 10.98; N, 4.36; Br, 24.86%. Mp 121—123 °C (123—124 °C[1]).

Found: C, 53.41; H, 9.68; N, 3.78; I, 32.95%. Calcd for $C_{34}H_{74}N_2I_2$ (n=10): C, 53.40; H, 9.75; N, 3.66; I, 33.19%. Mp 142.5—144 °C.

Fluoride solutions (C_nF_2) have been prepared by the triple decomposition of a mixture of BaF_2, Ag_2SO_4, and the corresponding bromide (or iodide) by using stoichiomet-

ric amounts of the latter two components and excess of the former.[20,22] When a small amount of bromide (or iodide) ion was found in the filtrate, an aqueous AgF solution, obtained by the neutralization of AgOH with an aqueous HF solution, was added, and the precipitated silver bromide (or iodide) was removed by either filtration (pore size 1.0 μm) or centrifuge (2000G, 30 min). Solutions of $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]Cl_2$ and $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]Y$ (Y=OOC-COO and OOC-$(CH_2)_3$-COO) (which we denote by C_6Cl_2, C_6Oxa, and C_6Glu hereafter) were prepared by neutralizing $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3](OH)_2$ ($C_6(OH)_2$) solutions with the corresponding acids. The hydroxide $C_6(OH)_2$ was obtained by treating a solution of C_6Br_2 with freshly prepared silver hydroxide, and purified by recrystallization from water[19,20,23] in the form of a clathrate hydrate crystal (see below). Both oxalic and glutaric acids were reagent grade commercial materials and recrystallized from water. The two fluoride solutions prepared by different methods (neutralization of $C_6(OH)_2$ with HF and triple decomposition of C_6Br_2 with BaF_2 and Ag_2SO_4) showed exactly the same behavior.

The experimental procedures for determing the solid-liquid phase diagrams for the binary mixtures of these salts with water were almost the same as in previous papers.[22,23] A sample solution (about 1.0—1.5 g) was prepared by weighing out water and a concentrated sample solution obtained by dehydrating a dilute solution using a rotary evaporator and whose water content was determined by the Karl Fischer titration method. No attempt was made to remove the air dissolved in the solution.

Results

The solid-liquid phase diagrams for the binary mixtures of water with C_4F_2, C_5F_2, C_6F_2, C_8F_2, and $C_{10}F_2$ are shown in Fig. 1, indicating that all the salts form hydrates which melt congruently and have large hydration numbers. The formation of these hydrates except for C_8F_2,[1] is confirmed for the first time. Judging from the large hydration numbers, the hydrates appear to be clathrate-like hydrates. The melting points and hydration numbers of these hydrates which have been read off each phase diagram are summarized in Table 1.

Table 1. The melting points and the hydration numbers of $[(C_4H_9)_3N(CH_2)_nN(C_4H_9)_3]F_2$ hydrates

n	Melting point (°C)	Hydration number
4 (stable)	2.8	39±3
4 (metastable)	−3.1	45±2
5	12.4	42±2
6	20.4	46±2
8	6.8	48±2
10	−2.2	50±2

The most appropriate methylene chain connecting the two terminal $(C_4H_9)_3N$ groups for the formation of a stable hydrate is a hexamethylene chain. The stability of the C_6F_2 hydrate (mp 20.4 °C) is comparable to that of several tetrabutyl (or isopentyl)ammonium salt hydrates.[20,22-24] The melting point and hydration number for the C_8F_2 hydrate are fairly different from those reported by Broadwater and Evans (5 °C and about 40).[1] A detailed comparison of the data is impossible because of the lack of experimental information. It has often been noticed that, for many tetraalkylammonium salt hydrates, the composition and the melting point of a hydrate which is separated from its solution phase and exposed to the atmosphere vary considerably with time.[22] Two types of hydrates (stable and metastable phases) have been found for the C_4F_2 salt. The stable phase has less water molecules (39±3) than the metastable one (45±2).

The effect of anions on the formation of clathrate-like hydrates has been examined for a series of C_6-compounds, whose cation is most suitable in size for the formation of stable hydrate as mentioned above. In Fig. 2 the solid-liquid phase diagrams for a series of C_6-compounds ($C_6(OH)_2$, C_6F_2, C_6Cl_2, C_6Br_2,

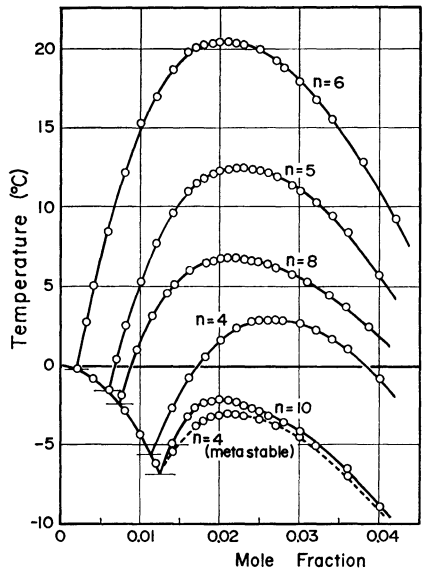

Fig. 1. The solid-liquid phase diagrams for the water + $[(C_4H_9)_3N(CH_2)_nN(C_4H_9)_3]F_2$ (n=4, 5, 6, 8, and 10) systems.

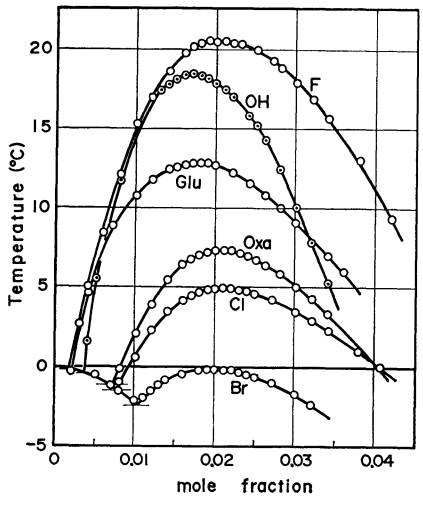

Fig. 2. The solid-liquid phase diagrams for the water + $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]$ (X_2 or Y) (X=OH, F, Cl, and Br; Y=OOC-COO and OOC-$(CH_2)_3$-COO) system.

TABLE 2. THE MELTING POINTS AND THE HYDRATION NUMBERS OF THE HYDRATES OF HEXAMETHYLENEBIS(TRIBUTYLAMMONIUM) AND TETRABUTYLAMMONIUM COMPOUNDS

Anion	Cation $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]^{2+}$		Cation $(C_4H_9)_4N^+$	
	Mp (°C)	Hydration number	Mp (°C)	Hydration number
Br^-	−0.2	48±3	12.5[a]	30.5,[a] 32.6[a]
Cl^-	4.9	47±2	15.0	28±3
			15.7[a]	32.1,[a] 33.8[a]
$(OOC-COO)^{2-}$	7.3	47±2	16.6[b]	58±1[b]
			16.8[a]	67,[a] 64[a]
$[OOC-(CH_2)_3-COO]^{2-}$	12.8	55±2	20.2[b]	55±1[b]
OH^-	18.4	58±2	28.0	33±1
F^-	20.4	46±2	28.3	31±1
			24.9[a]	32.8,[a] 34.0[a]

a) From Ref. 20. b) From Ref. 23.

C_6Oxa, and C_6Glu) are shown and indicates that all C_6-compounds examined form hydrates similar to those found in Fig. 1: characterized by their high water contents and congruent melting points. The melting points and hydration numbers obtained are summarized in Table 2, together with those of the corresponding tetrabutylammonium salts.

Discussion

The Effect of n *on the Formation of* C_nF_2 *Hydrates.* As can be seen from Fig. 1 and Table 1, C_6F_2 forms the most stable hydrate (mp 20.4 °C). From the fact that, in the clathrate hydrates of tetrabutyl(or isopentyl) ammonium salts, 7—8 water molecules are required in order to surround one butyl (or isopentyl) group, and that the C_6F_2 molecule has seven hydrophobic groups (six butyl groups and one hexamethylene chain), the hydration number of 46±2 observed for the C_6F_2 hydrate is a little bit smaller than expected. This indicates that the hydrogen-bonded water framework around the C_6F_2 molecule becomes efficient by the sharing of the common faces of adjacent polyhedra. Although the solution properties caused by the promotion of additional hydrogen bonding of the water molecules in the vicinity of the hydrocarbon groups have been studied exclusively in aqueous solutions of C_8Br_2,[1,3-5,7] the results here suggest that the structural effect in C_6-salt (and also C_5-salt) solution will be greater than that in C_8-salt solutions. The enthalpy of the $H_2O \rightarrow D_2O$ (and also $H_2O \rightarrow$propylene carbonate) transfer for C_8-cation clearly indicates that the structural effect for this ion in water is considerably smaller than that for two tetrabutylammonium ions.[5]

In Fig. 3, the melting points and hydration numbers of C_nF_2 hydrates have been plotted against n. It may be seen from the figure that both the melting points and hydration numbers vary differently with n depending upon whether n is smaller or larger than 6. When n is smaller than 6, both the melting points and the hydration numbers increase with increasing n, whereas when n is larger than 6, the melting points drastically decrease with increasing n while the hydration numbers increase in a similar manner as before but less sharply.

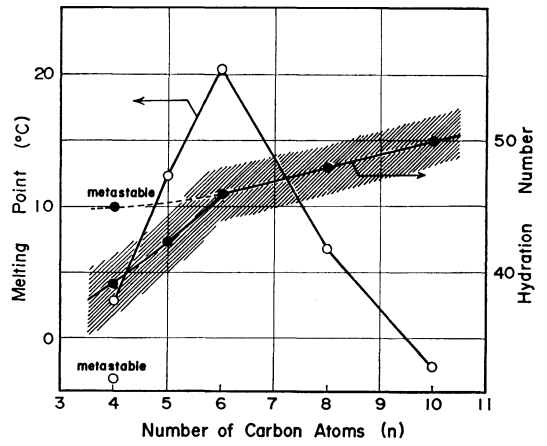

Fig. 3. The melting points and the hydration numbers of the $[(C_4H_9)_3N(CH_2)_nN(C_4H_9)_3]F_2$ hydrates as a function of n.

The hydration number of the metastable C_4F_2 hydrate lies approximately on the extention of the line for $n \geq 6$.

Although there is no evidence concerning the crystal structure of these hydrates, the following structure is consistent with the behavior shown in Fig. 3: the principal constituent of the hydrates may be considered as a clump consisting of three hydrogen-bonded water frameworks (presumably distorted tetrakaidecahedra or pentakaidecahedra) each of which surrounds one of the butyl radicals in the terminal $(C_4H_9)_3N$ group. This unit is schematically depicted in Fig. 4, with the assumption that each polyhedron is 14-hedron. The $(C_4H_9)_3N$-group sheath is denoted hereafter by 3P (P stands for polyhedron). The C_nF_2 hydrate crystal is then made up of two 3P's arranged face to face, in the interstitial space of which is accommodated a polymethylene chain, $-(CH_2)_n-$, which connects the two $(C_4H_9)_3N$-groups.

In the C_4F_2 hydrate (stable phase), the two 3P's are drawn together since they are covalently combined by a short polymethylene chain (the maximum distance between the two nitrogen atoms is 6.2—6.3 Å). The most probable configuration for this would be the

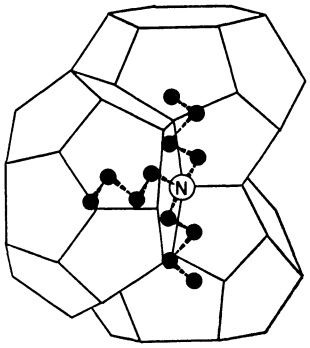

Fig. 4. The schematic representation of the water frameworks which enclathrate a $(C_4H_9)_3N$-group (3P).

twisted combination — a rotating 60° about the N–N axis as in the staggered ethane molecule conformation. The water framework within which the $-(CH_2)_4-$ chain is accommodated is automatically formed when the two 3P's approach, in agreement with the observation that the hydration number of the C_4F_2 hydrate is considerably small (39±3). The low melting point of this hydrate is presumably due to the strong distortion of the framework. The increase of both hydration number and melting point with increasing n from 4 to 6 is due to the formation of a larger and less distorted cage to accommodate a longer polymethylene chain ($-(CH_2)_5-$ and $-(CH_2)_6-$). In the compound C_6F_2, which gives the most stable hydrate, the stretched chain-length between the two nitrogen atoms, 8.8 Å, is very close to the average cage diameter of a typical polyhedron (8.7 Å for a 14-hedron and 9.4 Å for a 16-hedron[25]).

The slight increase in the hydration numbers and the drastic decrease in the melting points with increasing n from 6 to 10 reflects the situation that a few more water molecules are necessary to form a larger cage than in the case of C_6F_2 hydrate in order to accommodate the longer chain. Chain flexibility cancels this out to some extent, and furthermore the cage thus constructed is inevitably distorted compared with the most stable polyhedra such as the 14-hedron and 16-hedron. As to the structure of the metastable C_4F_2 hydrate, from the experimental results, *i.e.* a considerably low melting point and a hydration number (45±2) much larger than that in the stable phase (39±3) and position nearly on the extention of the line for $n \geq 6$ as previously pointed, it appears essentially similar to the structure for $n \geq 6$, but much more strained because of the short methylene chain. Presumably the two 3P's would take an eclipsed conformation in contrast to the staggered conformation which was assumed to be the stable phase as discussed earlier. Further detailed crystallographic studies of these hydrates are needed.

The Effect of Anion on the Formation of the C_6-Hydrates. The correlation between the melting points of the hydrates of C_6-compounds with various anions and those of the corresponding tetrabutylammonium compounds is shown in Fig. 5. This figure indicates two interesting facts: (1) the melting points of the C_6-compound hydrates are about 10 °C lower than those

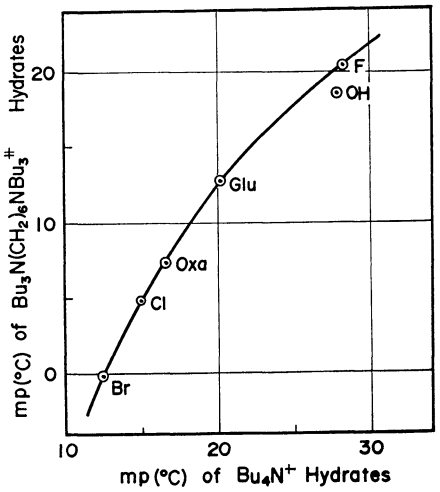

Fig. 5. The correlation between the melting points of the $[(C_4H_9)_3N(CH_2)_6N(C_4H_9)_3]^{2+}$ hydrates and those of the $(C_4H_9)_4N^+$ hydrates.

of the tetrabutylammonium compound hydrates irrespective of the type of anion; (2) there exists approximately linear relationship between the two sets of melting points. The former point emerges since the formation of the hydrogen-bonded water framework around the C_6-cation is considerably more difficult compared with the case of the tetrabutylammonium cation. The latter point indicates that the lattice distortion caused by the presence of the anion affects the stabilities of the hydrates in a similar manner in both series of salts. As may be seen from Table 2, all the C_6-compounds, except C_6Glu and $C_6(OH)_2$, have the same hydration numbers — around 47. This, suggests that they are isostructural, having a strong resemblance to the finding that the corresponding tetrabutylammonium salt hydrates are isomorphous (tetragonal).[20] The relatively large hydration number found for glutarate hydrate may be a consequence of the additional water molecules needed in order to surround the large $OOC-(CH_2)_3-COO$ anion, a striking contrast to the $[(C_4H_9)_4N]_2OOC-(CH_2)_3-COO$ hydrate which has a cosiderably small hydration number.[23] Hydroxide hydrate has also a large hydration number. A similar but less sharp trend is seen for tetrabutylammonium hydroxide hydrate and this may be due in part to the strong hydration of the hydroxide ion.

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