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Hydrogen bonding
Part 38. IR and thermodynamic study of phosphorylcholine chloride calcium salt tetrahydrate and monohydrate

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Abstract

Vapor pressure vs. H_2O content studies demonstrate that phosphorylcholine chloride calcium salt forms two hydrates, a monohydrate and a tetrahydrate, in the range 0-4 mol H_2O mol^{-1} of salt; there is no dihydrate or trihydrate. Equilibrium vapor pressure measurements show that ΔH^0 of dissociation per mol H_2O lost is greater for the tetrahydrate (16.08 kcal mol^{-1}) than for the monohydrate (12.49 kcal mol^{-1}); the lower stability of the tetrahydrate arises from entropy effects. The IR spectrum of the tetrahydrate is that of a framework clathrate hydrate and suggests that the $-PO_3$ group may act as a very weak hydrogen-bond acceptor. In the monohydrate the $-PO_3$ group is not involved in hydrogen bonding. Neither hydrate contains P-OH bonds.

INTRODUCTION

As an initial step in a program directed toward the study of hydration of model compounds for the head group of phosphatidylcholine we chose to examine the lower hydrates of phosphorylcholine chloride calcium salt (PCCCa). The objectives of this study were to examine hydrate stoichiometry through H_2O content vs. vapor pressure measurements and to determine thermodynamic parameters for the dissociation of hydrates by equilibrium vapor pressure studies. In addition we wished to examine the IR spectra of PCCCa hydrates to determine the extent to which the $-PO_3$ group might act as an acceptor to hydrogen bonds from H_2O.

EXPERIMENTAL

Phosphorylcholine chloride was obtained from Sigma (St. Louis, MO); NMR analysis [1] showed it to be a tetrahydrate (4.00 mol H_2O mol^{-1} salt). Anhydrous phosphorylcholine chloride was prepared by drying the tetrahydrate in vacuo at 60 °C over P_2O_5 for one week. The sample of the monohydrate used for the IR spectrum was taken from the vapor pressure cell after the water content had been reduced to the monohydrate level.

The vapor pressure apparatus has been described elsewhere [2]. IR spectra were recorded on a Perkin–Elmer Model 283 Spectrophotometer as Nujol mulls on CsI plates. The monohydrate and anhydrous samples were handled in an efficient glove box under dry N_2.

RESULTS AND DISCUSSION

Stoichiometry and thermodynamics

A plot of vapor pressure vs. H_2O content (Fig. 1) shows plateaus for the tetrahydrate and monohydrate, and the absence of a trihydrate or dihydrate. There is a significant fall off of pressure in the region between 2.5 and 1.0 mol H_2O mol^{-1} salt which may indicate a solid solution in this region, but no plateau which can be associated with a dihydrate.

In variable temperature studies both PCCCa·H_2O and PCCCa·$4H_2O$ gave excellent straight line plots of ln P^n vs. $1/T$ (Figs. 2 and 3). Thermodynamic values derived from these plots are shown in Table 1.

The enthalpy of dissociation of a higher hydrate to a lower hydrate cannot be used to estimate hydrogen bond strength or other forces binding H_2O in the higher hydrate, as the bonds in the lower hydrate will be of a different type [3]. It is better to consider the total dissociation of the higher hydrate, followed by reformation of the lower hydrate. Application of Hess's law shows that the total ΔH^0_{diss} for a higher hydrate is the sum of ΔH^0_{diss} for that hydrate and the ΔH^0_{diss} values for any lower hydrates [3]. This yields 64.33 kcal mol^{-1} for the enthalpy of dissociation of PCCCa·$4H_2O$ to PCCCa and $4H_2O$; or 16.08 kcal mol^{-1} per H_2O lost. This is significantly higher than the value of 12.49 kcal

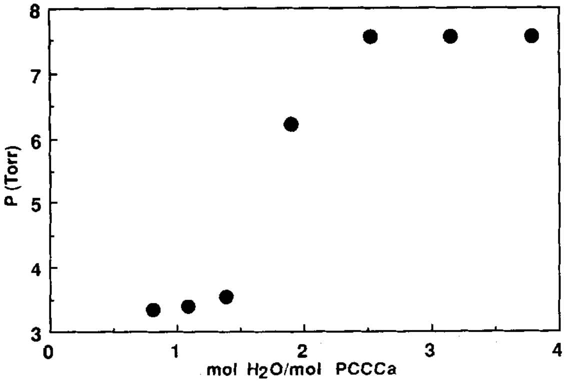

Fig. 1. Plot of H_2O vapor pressure over phosphorylcholine chloride calcium salt at 70 °C.

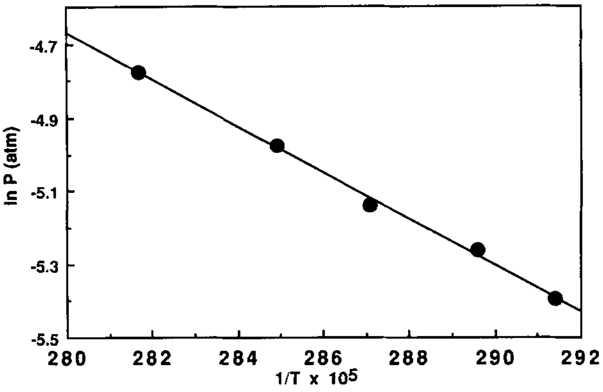

Fig. 2. Plot of ln P vs. $1/T$ for phosphorylcholine chloride calcium salt monohydrate.

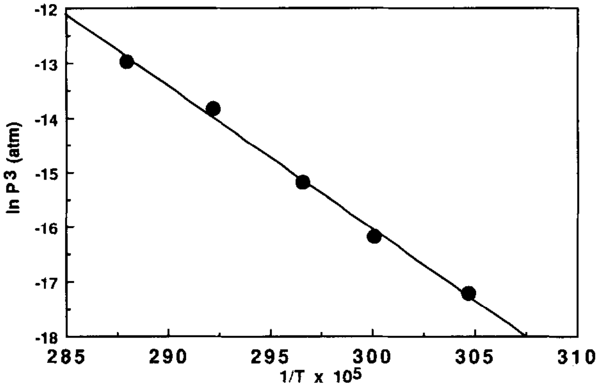

Fig. 3. Plot of ln P^3 vs. $1/T$ for phosphorylcholine chloride calcium salt tetrahydrate.

TABLE 1

Constants in the equations $\ln P^n = -(a/T) + b$ for phosphorylcholine chloride calcium salt (tetrahydrate and monohydrate) and derived thermodynamic data for the dissociation of these hydrates at 25 °C

Hydrate	H_2O lost $= n$	a	b	R^2	St. error	ΔG^0 (kcal mol^{-1})	ΔH^0 (kcal mol^{-1})	ΔS^0 (e.u.)
Tetrahydrate	3	26087	62.23	0.995	0.133	14.97	51.84	123.6
Monohydrate	1	6285	12.92	0.998	0.016	4.83	12.49	25.68

mol^{-1} found for loss of one mol H_2O from PCCCa·H_2O. PCCCa·$4H_2O$ is less stable than PCCCa·H_2O; that is, it develops higher pressures of H_2O over a lower temperature range (about 2.5–10 Torr at 55–74 °C) than PCCCa·H_2O does (about 3.5–6.5 Torr at 70–82 °C). This arises from the greater ΔS^0_{diss} per mol H_2O in PCCCa·$4H_2O$; hydrogen bonds or other intermolecular forces binding H_2O are stronger in the tetrahydrate than in the monohydrate.

It is not possible to apportion $\Delta H^0_{\rm diss}$ among the possible modes of binding H_2O in these hydrates in the absence of structural information. There are four possible hydrogen-bond acceptor sites (H_2O, Cl^-, $-PO_3^{2-}$ group and C–O–P oxygen), and H_2O may also be complexed by the Ca^{2+} ion. Since H_2O is likely to be at least as tightly complexed with Ca^{2+} in PCCCa·H_2O as in PCCCa·$4H_2O$, the extra $\Delta H^0_{\rm diss}$ per mol H_2O in the tetrahydrate presumably comes from stronger hydrogen bonding, but we cannot at this time determine precisely which hydrogen bonds are involved.

IR spectra

The IR absorptions associated with bound H_2O in PCCCa·H_2O and PCCCa·$4H_2O$ are listed in Table 2. The spectrum of PCCCa·$4H_2O$ is that of a typical framework clathrate hydrate, in which H_2O and anionic sites form an extended structure. The presence of two stretching absorptions indicates that both stronger and weaker hydrogen bonds are present. However, the relatively high frequency for ν_s H–O–H and the low frequency for ν_r H–O–H demonstrate that such hydrogen bonds are not particularly strong. The H_2O molecule in PCCCa·H_2O is very weakly hydrogen bonded, if at all; ν_s H–O–H is at 3400 cm^{-1}, and ν_r H–O–H, the librational mode characteristic of hydrogen-bonded H_2O, cannot be observed. With the additional fact that H_2O in PCCCa·H_2O is not interacting with the $-PO_3$ group (see below), we conclude that H_2O in PCCCa·H_2O is primarily complexed by Ca^{2+}, with the possibility of very weak hydrogen bonds to Cl^-.

As we have noted before [4,5], it is sometimes useful to discuss the vibrations of a portion of a molecular structure in terms of the local symmetry of that region. The local symmetry of the phosphorus atom and the four oxygens attached to it in PCCCa is C_{3v}, since three oxygens are identical and one (the ester oxygen) is different. The absorptions associated with P–O vibrations in

TABLE 2

Infrared absorptions associated with H_2O vibrations in phosphorylcholine chloride calcium salt and its hydrates[a,b,c]

Vibration	Assignment	PCCCa·H_2O	PCCCa·$4H_2O$
ν_s H-O-H	H-O-H stretch	3430, 3230 bvs	3400 bm
ν_b H-O-H	H-O-H bend	1680 sh, 1605 s	1650 w
ν_r H-O-H	H-O-H rock	630 bs[d]	[e]

[a]Units are cm^{-1} (wavenumbers). [b]Nujol mulls on CsI plates. [c]Symbols used: s, strong; m, medium; w, weak; b, broad; v, very; sh, shoulder. [d]Partially masked by P–O absorptions. [e]Not observed.

PCCCa·$4H_2O$, PCCCa·H_2O and anhydrous PCCCa are listed in Table 3, and are assigned for the purposes of this discussion under local C_{3v} symmetry. Since the phosphorylcholine anion very likely assumes a conformation in which the C–N and C–O bonds are gauche about the C–C σ-bond [6] the actual symmetry of the molecule would be C_1. However, the principal absorptions of the PO_4 subunit would be those allowed by the local symmetry, which are expected to have the greatest transition dipole moments [7].

The assignments listed in Table 3 were derived by consideration of how the known vibrational modes of the PO_4^{3-} ion [8] would be expected to change as symmetry changes from T_d to C_{3v} [9], and are in good agreement with assignments made on a large number of R–PO_3 species [10]. There is some debate over the assignment of the C–O–P stretching mode; our assignment is similar to that of Nyquist [11]. Proton transfer from H_2O to the phosphorus oxygen has not occurred in either hydrate as there are no absorptions in the 2700–2500 cm^{-1} region assigned to P–OH bonds (for a review see ref. 10).

Examination of the IR spectra of PCCCa·H_2O and anhydrous PCCCa (Fig. 4B and C; Table 3) shows that the absorptions associated with P–O vibrations are essentially superimposable on each other. There is no indication that the –PO_3 group in PCCCa·H_2O is in any way perturbed by the presence of the H_2O molecule, and we therefore assume that hydrogen bonding between the –PO_3 group and H_2O is entirely absent in this compound.

In contrast to the case with PCCCa·H_2O, the P–O absorptions of PCCCa·$4H_2O$ (Fig. 4A, Table 3) are different in appearance, though similar in overall pattern, from those in anhydrous PCCCa. The –PO_3 stretching frequencies, $\nu_5(e)$ and $\nu_1(a_1)$, which are blurred together in the anhydrous salt, are sharply cleaved from each other, and a similar effect is observed for the pair of z component bends, $\nu_6(e)$ and $\nu_3(a_1)$. In addition $\nu_4(e)$ is resolved into two bands. This suggests that the motions of the –PO_3 group are perturbed by

TABLE 3

Infrared absorptions associated with P–O vibrations in phosphorylcholine chloride calcium salt and its hydrates[a,b,c]

Vibration	Assignment	PCCCa anhyd.	PCCCa·H_2O	PCCCa·$4H_2O$
$\nu_5(e)$	unsym. PO_3 stretch	1140 sh	1140 sh	1150 vs
$\nu_1(a_1)$	sym. PO_3 stretch	1090 bvs	1095 bvs	1085 vs
$\nu_2(a_1)$	C–O–P stretch	950 bs	960 bs	965 vs
$\nu_6(e)$	unsym. PO_3 bend (z)	550 bs	560 bs	540 s
$\nu_3(a_1)$	sym. PO_3 bend (z)	510 sh	515 sh	510 s
$\nu_4(e)$	unsym. PO_3 bend (x,y)	410 bw	440 bvw	450 w, 410 w

[a] Units are cm^{-1} (wavenumbers). [b] Nujol mulls on CsI plates. [c] Symbols used: s, strong; m, medium; w, weak; b, broad; v, very; sh, shoulder.

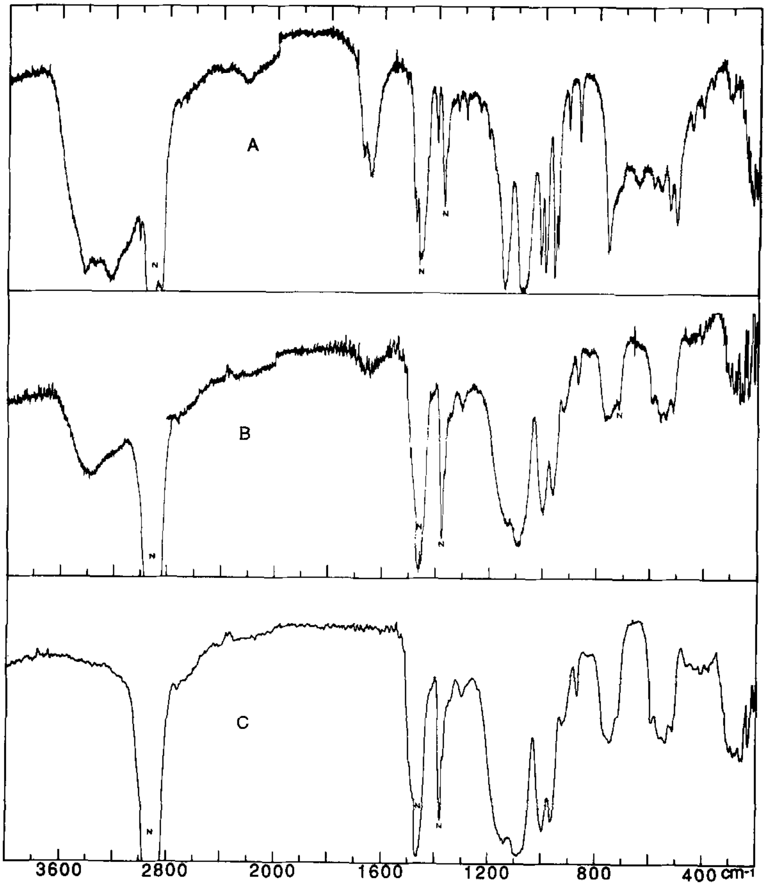

Fig. 4. IR spectra (Nujol mulls on CsI plates) of phosphorylcholine chloride calcium salt and its hydrates; A, tetrahydrate; B, monohydrate; C, anhydrous salt. Peaks marked N are from Nujol. Units are cm^{-1} (wavenumbers); %*T*.

the presence of H_2O, which may indicate that this group acts as an acceptor to hydrogen bonds from H_2O. The inconsequential frequency shifts of the stretching modes, however, indicate that such hydrogen bonds, if present, are quite weak.

All hydrogens in $PCCCa \cdot 4H_2O$ are involved in hydrogen bonding, as there is no absorption for free –OH. In $PCCCa \cdot 4H_2O$ there are eight hydrogens available to form hydrogen bonds, and eight acceptor sites (nine if the C–O–P oxygen is included). Thus it is theoretically possible for each H_2O, each $-PO_3$ oxygen and the Cl^- ion to act as an acceptor to a single hydrogen bond. Since halide ions normally act as multiple hydrogen-bond acceptors in framework clathrate hydrates the above arrangement seems somewhat unlikely. It is more likely that some H_2O and/or $-PO_3$ oxygens are not acting as acceptors to hydrogen bonds.

CONCLUSION

Phosphorylcholine chloride calcium salt forms two hydrates; a tetrahydrate and a monohydrate. Hydrogen-bonding and ion–dipole forces binding H_2O in the tetrahydrate are stronger than in the monohydrate; the lesser stability of the former compound arises from entropic effects. IR studies show that the H_2O molecule in the monohydrate is clearly not hydrogen-bonded to the $-PO_3$ group. Perturbation of the IR absorptions of the $-PO_3$ group in the tetrahydrate may arise from hydrogen bonding from H_2O; however, if such bonding is present it is very weak.

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