It appears, therefore, that the variations in the enthalpy of sublimation depend primarily on the lattice energy of the solid iodides.

Conclusions

The vapor pressures of all of the lanthanide triiodides are similar in the Knudsen cell range. The difference between that for CeI_3, the lowest, and that for TmI_3, the highest, is only threefold. The vapor pressures of the triiodides are appreciably higher than the more ionic bromides, chlorides, and fluorides.

Contrary to the usual consensus, the enthalpies of sublimation do not decrease monotonically with the atomic number of the lanthanides.

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Polymorphic Effects of Chloramphenicol Palmitate on Thermodynamic Stability in Crystals and Solubilities in Water and in Aqueous Urea Solution

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The differences in enthalpy and Gibbs free energy between α- and β-forms of crystalline chloramphenicol palmitate are determined in the temperature range of 36–130°C. A radiotracer method is applied for determining extremely low solubilities of the tritiated crystals in contact with water and 4 mol/l. urea solution at 20–35°C. All these results are discussed from the aspect of regular solution treatment, taking account of different sizes and shapes of these molecules in a polymorphic relationship.

For a quantitative understanding of the nature of insoluble monolayers at air–water interfaces, much information is needed on the thermodynamic data of the monolayer-composing compounds in three-dimensional crystals and in aqueous solutions (*8*). It has been shown previously (*9*) that the time-dependent character of the monolayer of chloramphenicol palmitate (CPP) is explicable by the conformational change of cis- → trans-molecules in two-dimensional crystal and that the change may correspond to the polymorphic transformation of CPP-$\alpha \rightarrow$ -β in three-dimensional crystal (*2, 17, 18*). These results are in qualitative agreement with the experimental results on crystalline structure (*1, 17, 18*), latent heat of fusion (*3, 15*), and dilatometric behavior (*2*) of CPP crystals. However, few papers have yet dealt with the thermodynamic stabilities of CPP in its crystalline states; nor has it been clarified where the transition temperature for $\alpha \rightleftarrows \beta$ transformation exists.

Additional information is definitively required on the interaction energy between CPP and water molecules, which is obtainable from the solubility data of CPP in aqueous media. Generally, however, the solubility in water is predicted to be so low as to make it possible to obtain stable monolayers on aqueous subphases. For such a sparingly soluble compound, it is always a problem to confirm the equilibrium for obtaining the solubility C_s from a gradual increase of concentration C with time t elapsed from the first contact of the solute substance with the solvent (*11, 12*). The flat portion of the $C \sim t$ relationship can hardly be determined. The ampul method (*16*) is not applicable to a sparingly soluble substance because of the perplexity in confirming the disappearance of an excess amount of the solute under a constant rate of temperature rise or at a constant temperature with varied time.

Krause and Lange (*10*) proposed a method based on the asymptotic approach of $C \sim t$ curves for under- and super-saturated solutions. For CPP, however, the polymorphic effect may cause incomplete merging of the two curves. It would be more reasonable to estimate C_s by putting $t = \infty$ in an appropriate rate equation for the dissolution process (*4–6*). Such an extrapolation method has been applied in the present study to determine the solubilities of CPP-α and -β in aqueous media by means of the radiotracer technique.

Experimental

Materials. The sample of CPP-^{3}H (Figure 1) was synthesized by condensation (*9*) of chloramphenicol and palmityl-2,3-^{3}H chloride, which was obtained by chlorination of the tritiated product of hexadecenoic acid (*14*).

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The purifications were repeated at each stage of the synthetic route, from tetradecanal to CPP-^{3}H, until a sample gave a single peak on the gas- or thin-layer chromatogram. The radiochemical purity was confirmed by radio gas chromatography for a methylated sample of palmityl-2,3-^{3}H chloride. The final sample of CPP-^{3}H (specific activity, 13.0 mCi/mmol) was of the β-form when recrystallized from benzene (*9, 17*). The sample of CPP-^{3}H-α was obtained by rapid pouring of CPP-β solution in acetone at about 50°C into ice water at 2°C. To obtain uniformly sized particles, fractional sedimentation was repeated several times in a cold mixture of acetone and water (1:9 in volume ratio) for CPP-^{3}H-α and in cold benzene for -β. Microscopic observation showed that the size of the crystalline particles was in the range of 0.2–0.6 μ for all of the CPP samples. A similar procedure was applied to obtain the samples of nonradioactive CPP-α and -β for thermal analysis.

All these samples were properly identified by X-ray diffraction, ir absorption, and melting-point determination (*17, 18*), and the purities were confirmed by the method described previously (*9*).

Apparatus and procedures. The calorimetric experiments were carried out with a differential scanning calorimeter (Rigaku Denki Co., Tokyo, Model 8050) in a temperature range of T = 36 – 130°C at a constant rate of 5°C/min for temperature rise. The rate of heat absorption for a CPP sample was calibrated with a standard sample of pulverous α-alumina, for which the molar specific heat C_p has well been established (*7*).

Because of hydrophobicity and rather small density (1.27 g/ml for CPP-α and 1.31 for -β), the CPP particles for solubility measurement were apt to adhere to the wall of the glass vessel while they were suspended in aqueous solvent under mechanical stirring. To avoid such adherence, the suspension of CPP-^{3}H (3.6 ± 0.2 mg) in an aqueous solvent (300 ml) was vigorously shaken in a glass ampul (5.5 cm in diameter and 20 cm in length) having a ground glass stopper at the shoulder. The container was sunk in a thermostat of ±0.02°C and vertically reciprocated with an amplitude of about 10 cm and a rate of 230 strokes/min.

At a given time t, an 0.5–2-ml portion of the solution was pipeted through a glass tip covered with a piece of filter paper. Comparative tests indicated that reproducible results were always obtained by the use of Toyo Filter Paper #4 when it had been dipped in the solvent for 24 hr prior to pipeting. Swelling of the paper fiber could be helpful to remove the colloidal material which seemed to be one of the factors responsible for experimental scattering (*10, 13*).

Another difficulty was involved in the adsorption of solute at the paper/solution and glass/solution interfaces made freshly available upon pipeting (*10*). To eliminate such an adsorption effect, it was found sufficient to discard the first five crops obtained with a set of pipet, tip, and filter paper. The sixth aliquot was transferred into a stainless-steel planchette and evaporated to dryness at below 60°C by irradiation with an infrared lamp. For the ternary mixture of CPP, urea, and water, the radioactive solute was extracted with toluene for transfer into the planchette. The radioactivity was determined with a 2 π windowless gas-flow counter (Aloka, Model TDC 1) and corrected appropriately for self-absorption and self-scattering. It was finally calibrated with standard samples for conversion into the concentration C in mol/l.

Results

The latent heats of fusion, $\Delta H_2{}^f$, obtained for crystalline CPP-α and -β from their peak areas in the calorimetric charts are summarized in Table I. The results are in agreement with the reported values (*3, 15*) cited in the last two lines.

From the $C_p \sim T$ relationships for CPP-α and -β in addition to the data in Table I, we could calculate the temperature dependence of molar enthalpy H relative to the transition point if it were known. No data, however, have yet been established for the temperature of CPP-$\alpha \rightleftarrows$ -β transition (*2, 15*). The melting point T_β (=364K) of CPP-β was temporarily taken for the standard temperature at which the two crystalline samples were commonly in the molten state. The molar enthalpy H (=0 at $T = T_\beta$) is thus plotted against T in Figure 2. The Gibbs free energy dissipation, $-\Delta G_\alpha{}^\beta$, for transformation from CPP-α to -β was calculated by the Gibbs-Helmholtz equation applied to the entire range of 36–91°C and is plotted in Figure 3 against T.

In Figure 4 the symbols express the experimental $C \sim t$ relationships for CPP-α and -β in contact with water and with an aqueous urea solution of 4 mol/l. It has been shown by many investigators (*4–6*) that the rate of dissolution is expressed as

$$dC/dt = k(C_s - C)^n \qquad (1)$$

where C_s is C at $t = \infty$, k is the rate constant, and n is the order of the dissolution process. For $n \geqq 2$, however,

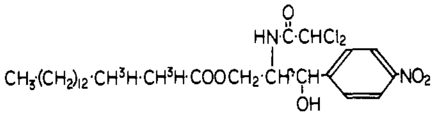

Figure 1. Structure formula of chloramphenicol palmitate-2,3-^{3}H (CPP-^{3}H)

Table I. Latent Heats of Fusion ($\Delta H_2{}^f$ in kcal/mol) of CCP-α and -β

CPP-α, mp, 359K	CPP-β, mp, 364K	Ref
11.28	17.48	Present work
11.35	17.54	
11.37	17.58	
11.39	17.63	
11.42	17.68	
Av 11.36 ± 0.08	17.58 ± 0.10	
11.5 ~ 12.4	16.3 ~ 17.2	(15)
10.4	15.3	(3)

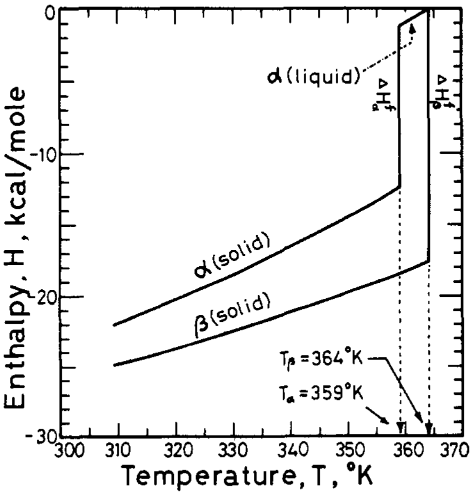

Figure 2. Temperature dependence of enthalpy H of CPP-α and -β

none of the experimental results satisfied Equation 1. For $n = 1$, the equation becomes

$$-kt = \ln(1 - C/C_s) \tag{2}$$

In the region of $C \ll C_s$, Equation 2 is rewritten by

$$\frac{1}{C} = \frac{1}{kC_s}\frac{1}{t} + \frac{1}{C_s} \tag{3}$$

The intercept of the $1/C \sim 1/t$ plot gave the first approximation of $1/C_s$. Starting with this, successive approximation was continued until a good proportionality was obtained between t and $\log(1 - C/C_s)$ by the use of an appropriate C_s value. Table II summarizes such solubility values as a function of T. In Table III the second and the third columns give the activation energy ΔE and the frequency factor k_0, respectively, obtained from the linear relationship between $\log k$ and $1/T$ (top of Figure 5). In Figure 4 the curves express the $C \sim t$ relationships reproduced by

$$\ln(1 - C/C_s) = -k_0 t \exp(-\Delta E/RT) \tag{4}$$

for a set of k_0 and ΔE values (Table III) and $T \sim C_s$ relationship (Table II). Fairly good agreement between calculated (curves) and the observed (symbols) C values indicates the appropriateness of C_s values shown in Table II.

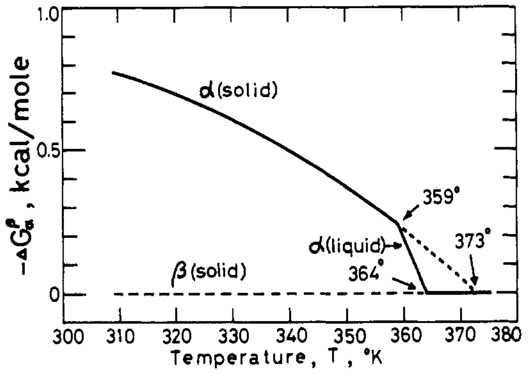

Figure 3. Gibbs free energy difference, $-\Delta G_\alpha^\beta$, plotted against T

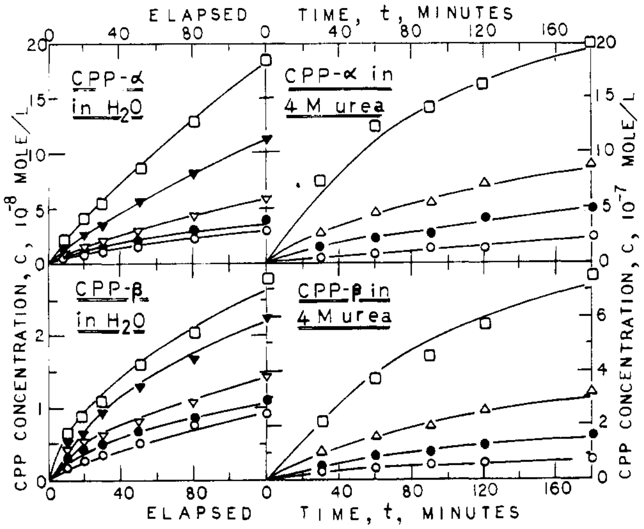

Figure 4. $C \sim t$ relationships for CPP-α (top figures) and -β (bottom) in water (left) and in 4 mol/l. urea solution (right) at 20°C (○), 25°C (●), 29°C (▽), 30°C (△), 32°C (▼), and 35°C (□). Symbols denote experimental results, and curves express time dependence of C calculated by Equation 4, using C_s values in Table II and ΔE and k_0 values in Table III

Table II. Solubilities (C_s, in 10^{-8} mol/l.) of CPP-α and -β in Water and in Aqueous Urea Solution (4 mol/l.) as Function of Temperature T

	Water		Urea solution	
T, °C	CPP-α	CPP-β	CPP-α	CPP-β
20.0	8.5	1.1	35.0	8.9
25.0	9.6	1.5	68.0	18.6
29.0	14.4	1.8	...	...
30.0	...	...	110	36.1
32.0	26.0	2.7	...	...
35.0	38.0	3.1	249	85.0

Discussion

From Figure 3, crystalline CPP-α is less stable than -β throughout the whole temperature range, 36-91°C, giving $-\Delta G_\alpha^\beta = 0$ either at 364K or at 373K. The former is the case of reality, whereas the latter is the imaginary case that the solid CPP-α was not to melt below the temperature. The crystalline CPP-α must thus be in a metastable state with regard not only to enthalpy (Figure 2) but also to Gibbs free energy (Figure 3). In plotting dilatometric curve against temperature, Aguiar (2) observed a marked kink at 77°C, which was ascribed not to transition, but to enhanced reversion of polymorphic change from metastable CPP-α to stable -β. It is obvious from Figures 2 and 3 that the CPP molecules in α-form, in comparison with β-, are characterized by a high energy and a disordered lattice structure. At 36°C, for example, the polymorphic transformation from CPP-α to -β was found to accompany decreases in G, H, and entropy in the amounts of 0.77 kcal/mol, 2.79 kcal/mol, and 6.5 eu, respectively. This kind of feature must be revealed in the spontaneous transformation of crystalline CPP-α to -β while the former is kept in storage.

The results shown in Table II reveal that CPP-α is more hydrophilic than -β and that the addition of urea to the aqueous medium affects more markedly the solubility of CPP-β than that of CPP-α. These findings imply that the solubility difference between the polymorphic crystals would be interpreted in terms of the pair-interchange energy Φ defined as

$$\Phi = \epsilon_{12} - (\epsilon_{11} + \epsilon_{22})/2 \tag{5}$$

where ϵ_{12}, ϵ_{11}, and ϵ_{22} are the bond energies for CPP-solvent, solvent-solvent, and CPP-CPP pairs as the binding units in solution. Let us consider a regular mixture of n_1 moles of a solvent and n_2 moles of CPP. Dissimilarities in size and shape between solvent and CPP molecules (kinetic unit of individual species) are represented by the difference between the numbers, z_1 and z_2, respectively, of the nearest neighbors. If we denote by p_2 the fraction of z_2 contributed by CPP-solvent linkage, the chemical potential μ_2 of CPP in the solution is given approximately by

$$\mu_2 = \mu_2^l + z_2 N\Phi\left[p_2 + \frac{\partial p_2}{\partial(\ln n_2)}\right] + \ln x_2 \tag{6}$$

where μ_2 is the chemical potential of pure CPP in the molten state; N, the Avogadro number; R, the gas constant; T, the temperature; and x_2, the mole fraction of CPP in the mixture. Assuming that p_2 is independent of n_2, the equality of μ_2 to the chemical potential of crystalline CPP leads to

$$\ln x_2^s = -\Delta H/RT + \text{constant} \tag{7}$$

with

Table III. ΔE, k_0, ΔH, and $p_2z_2N\Phi$ **Values for CPP-α and -β in Water and in Urea Solution (4 mol/l.)**

	Activation energy, ΔE, kcal/mol	Frequency factor, k_0, min^{-1}	Heat of solution, ΔH, kcal/mol	Molar interchange energy, $p_2z_2N\Phi$, kcal/mol
		Water		
CPP-α	4.0	3.31	+20.0	+8.6
CPP-β	4.8	36.5	+13.7	−3.9
		Urea solution		
CPP-α	7.4	1.78×10^3	+22.9	+11.5
CPP-β	1.6	0.145	+26.7	+9.1

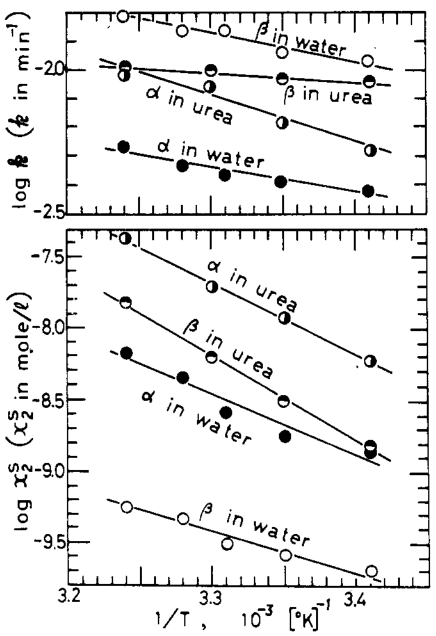

Figure 5. Effects of $1/T$ upon $\log k$ (top figure) and $\log x_2{}^S$ (bottom) for CPP-α and -β in water and in urea solution (4 mol/l.)

$$\Delta H = \Delta H_2{}^f + p_2z_2N\Phi \qquad (8)$$

where $x_2{}^s$ is the solubility (in mole fraction) of CPP in one of the crystalline states, and ΔH its heat of solution. In Table III the fourth column lists the ΔH values based on the $\ln x_2{}^s \sim 1/T$ relationship in the bottom of Figure 4. Using our $\Delta H_2{}^f$ values in Table I, the molar interchange energy $p_2z_2N\Phi$ is calculated to list in the last column of Table III. Note that all these data are based on the tacit assumption that the molecular conformation of CPP was to remain unchanged in the solution throughout the dissolution processes, because C_S in Table II was obtained as C at $t \rightarrow \infty$ in Equation 2.

For the CPP-water system, the adhesive energy, ϵ_{12} in Equation 5, is larger for CPP-α and smaller for -β than the sum of the cohesive energies, $(\epsilon_{11} + \epsilon_{22})/2$. Thus, the change from hydrophilic CPP-α to hydrophobic -β in aqueous solution must accompany an energy dissipation in the amount of

$$\Delta(p_2z_2N\Phi)_\alpha{}^\beta = N\{(p_2z_2\Phi)_\beta - (p_2z_2\Phi)_\alpha\} = -12.5 \text{ kcal/mol} \qquad (9)$$

This could be contributed by a decrease either in Φ or, more possibly, in p_2z_2, number of sites available for binding to water. The regular solution treatment essentially requires an excess (intramolecular) entropy to be convertibly involved in the excess energy term. The process to increasing hydrophobicity must be followed by precipitation of CPP-β, because its solubility is much lower than that of CPP-α (Table II). This is the case for spontaneous transformation of crystalline CPP-α to -β when its aqueous suspension is kept standing for a long time. A similar explanation could be given to the spontaneous change of the nature of CPP monolayer at the air-water interface (9).

It is noteworthy that the energy dissipation, $\Delta(p_2z_2N\Phi)_\alpha{}^\beta = -2.4$ kcal/mol, for the CPP-urea solution system is much smaller than that for the CPP-water system. This should be ascribed to an increase of Φ rather than p_2z_2 for CPP-β. In fact, the reversion of the energy sign for CPP-β can no more be explicable by an increase of p_2z_2. It is probable that the highly ordered assembly of a CPP-β molecule, in comparison with -α, is characterized by its sites freshly available for 1-2 linkage(s) upon addition of urea to water.

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