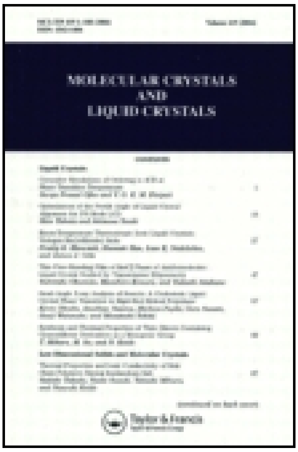

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Thermal Behaviours of Inclusion Compounds of Cholic Acid

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THERMAL BEHAVIOURS OF INCLUSION COMPOUNDS OF CHOLIC ACID.

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Abstract Inclusion complexes of cholic acid with acetophenone, methanol and ethanol have been studied by thermoanalytical methods (TG-DTA-MS, DSC, DRC-TG). Liberation processes of the guest molecules were not a single step. The initial elimination reaction was assigned to the first order decay. The elimination temperatures and their activation enthalpies are determined.

INTRODUCTION

Cholic acid (3α, 7α, 12α-trihydroxy-5β-cholan-24-oic acid) forms various types of inclusion complexes with many kinds of organic compounds. The structures of complexes of cholic acid with alcohols, carboxylic acids, ketones, esters and etc. have been studied by x-ray diffraction$^{1-4)}$. In this paper, thermal behaviour of cholic acid and those of its inclusion complexes of methanol, ethanol and acetophenone have been studied by TG-DTA-MS and dynamic DRC-TG$^{5)}$.

EXPERIMENTAL

Inclusion complexes of cholic acid with methanol, ethanol, and acetophenone have been synthesized by recrystallization from the purified guest solvents. The inclusion complexes obtained were dried under vacuum(10^{-1} to 10^{-2} Pa) at ambient temperature, then heated at temperatures lower than the first elimination temperatures by 5 K, over 6 hours. It is very important that the inclusion compounds are free from adsorbed guest solvents on crystal surfaces. The inclusion compounds obtained by the above mentioned procedure did not show any abnormal thermograms (TG-DTA, DSC) from ambient temperature. Cholic acid(without guests) was recrystallized in pure acetone at higher temperatures than 313 K. The guest molecules were purified by rectification. G.l.c. results of the guest solvents showed merely some trace-impurity peaks ($<10^{-7}$). Coulometric Karl-Fischer's method on a Moisturemeter gave the water content of each solvent to be 0.01 mole per cent or less.

Thermogram of inclusion complexes of cholic acid with methanol, ethanol and acetophenone and those of pure cholic acid have been determined by TG-DTA-MS (Rigaku, TG8101), DSC (Rigaku, DSC8270A), dynamic rate control thermogravimetry (Rigaku, DRC-TG) from ambient temperature to 700 K. The scanning rates of TG-DTA and DSC was below 60 K/h except few measurements. X-ray diffraction of the powder samples were measured at ambient temperature. Standard mass chromatogram of acetophenone were determined by a high performance mass spectrometer (JEOL, JMS-HX100).

RESULTS AND DISCUSSION

Each example of TG curves of the inclusion complexes of cholic acid with methanol, ethanol and acetophenone is shown in Fig. 1. Elimination processes of guest molecules from the inclusion compounds of methanol and acetophenone showed clearly two or more steps during low scanning rate (below 30 K/h). Corresponding DTA and DSC curves also showed more than two peaks. The DRC-TG was successful in separating the first elimination process from other steps as shown in Fig. 2.

The elimination process of inclusion compound of acetophenone consists in two or more steps as shown in the TG-DTA curves in Fig. 3. A total ion chromatogram and mass chromatogram with TG-DTA of the inclusion compound of acetophenone are shown in Fig. 3. The total ion chromatogram also showed multi step eliminations. Mass chromatogram (c-1, c-2) of mark 1 and 2 in total ion chromatogram(b in Fig. 3) showed only parent ion and fragments of acetophenone. The mass chromatogram agreed with that of pure acetophenone by high performance mass spectrometer. The mass spectrometry showed that the evolved gases obtained from the inclusion

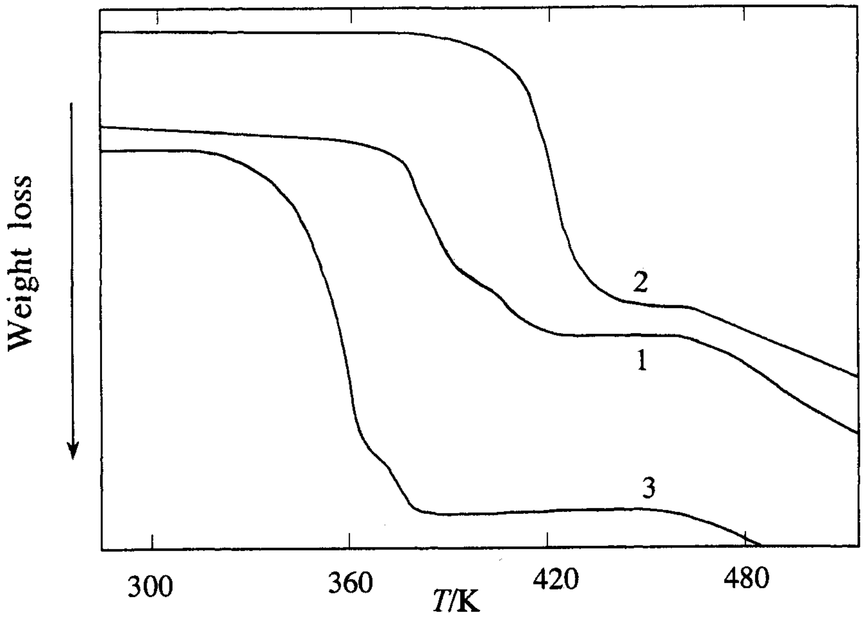

Figure 1 TG curves of the inclusion complexes of cholic acid. Guest molecules: 1, methanol; 2, ethanol; 3, acetophenone.

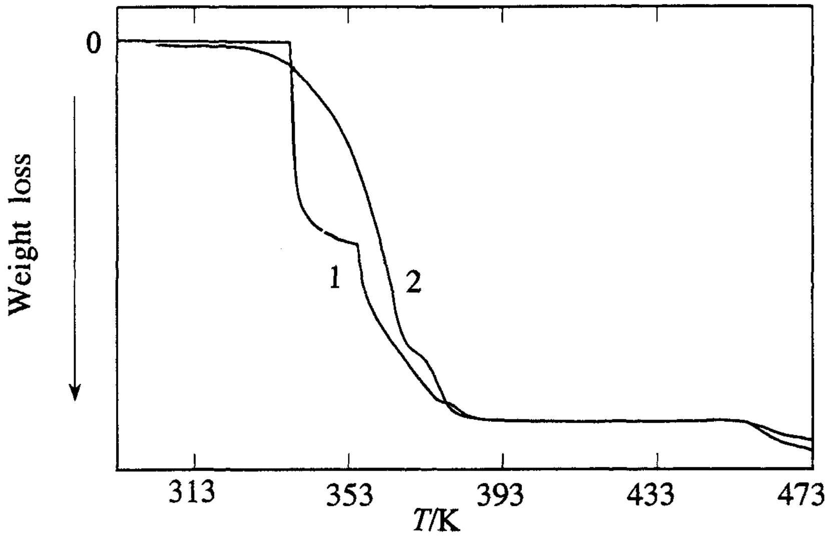

Figure 2 Comparison of DRC-TG and TG curves of the inclusion complex of acetophenone: 1, DRC-TG curve; 2, TG curve.

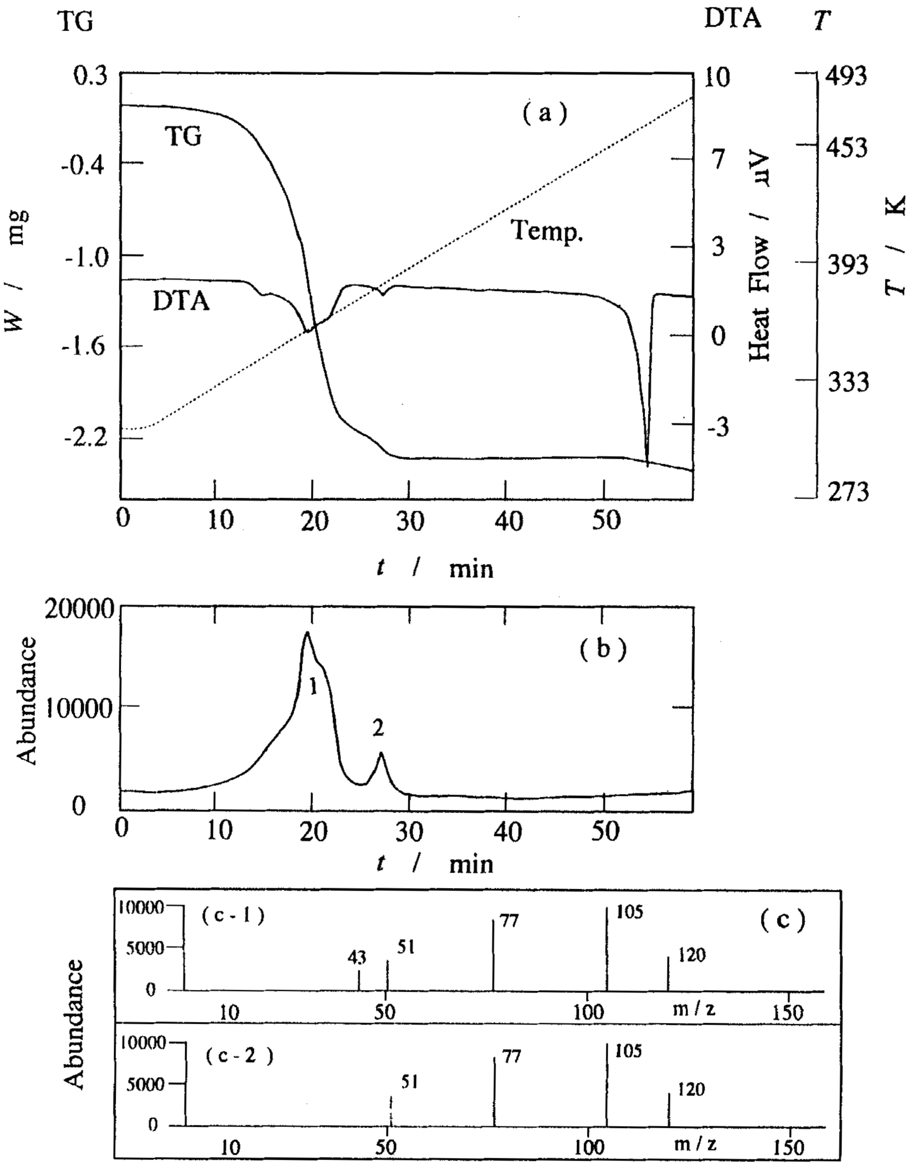

Figure 3 TG-DTA curves and mass spectrum of the inclusion complex of acetophenone: a, TG-DTA curves; b, Mass chromatogram; c, mass spectra: c-1 and c-2 are mass spectra at point 1 and 2 in b, respectively.

compounds during whole elimination steps were only the guest molecule of acetophenone.

The inclusion complexes of methanol which showed two or more stepwise elimination gave the same mass chromatogram. The elimination and transition temperatures and enthalpies of elimination of guest molecules from the inclusion compounds and enthalpies of fusion of inclusion compounds were summarized in Table 1 as well as pure cholic acid. All the temperatures and enthalpies in Table 1 were determined by extrapolation to zero scanning rate and sample mass except those of melting of the inclusion compounds. The elimination temperature of the inclusion compound of acetophenone was lower than those of inclusion compounds of ethanol and methanol.

Table 1 Thermal properties of the inclusion compounds of cholic acid

guest molecule			P_1	P_2	P_3	P_4	Ea kJ mol^{-1}	r
	DTA	T	333.0	347.2	435.2	459.0		
acetophenone		ΔH	28.1	4.01	-3.51	32		
	TG	Δw	21.5		0	0	99.1	0.961
methanol	DTA	T	374.2	385.4		477.6		
		ΔH	10.49	4.62		32		
	TG	Δw	6.14		0	0	94.1	0.991
ethanol	DTA	T	388.5			458.5		
		ΔH	33.77			22		
	TG	Δw	6.5		0	0	137.5	0.999
none	DTA	T				455.8		
		ΔH				31.5		
	DSC	T				455.5		
		ΔH				31.6		

P_i's are elimination temperatures and melting point in K. ΔH is enthalpy in kJ·mol^{-1}. ΔW is weight loss with elimination of guest molecules in %. P_1, the first elimination temperature; P_2, the second elimination temperature; P_3, transition temperatures of "empty" cholic acid to stable form; P_4, melting temperature of inclusion complex; Ea, activation energy of elimination of the first step; r, correlation coefficient for determined reaction type.

The crystal structure of inclusion compound of cholic acid with acetophenone and alcohols are, respectively, channel[1)] type and non-channel(cross over) [3)] type. The channel structure might be easy to release the guest molecules from the complex.

The elimination reaction of guest molecules was analyzed by Ozawa method[6,7)]. The experimental reaction rates were obtained at various temperatures and different heating rate of 20, 30, 45, 50 and 60 K/h. The activation energies of elimination of guest molecules were determined and listed in Table 1. The activation energy of elimination of ethanol from the inclusion compound was 40 to 50 % larger than anothers. All elimination rates were fitted with eight type reaction scheme[7)] of $(1\text{-}C)$, $(1\text{-}C)^n$, $C(1\text{-}C)$, $1/2C$, $-\ln(1\text{-}C)$, $2/3((1\text{-}C)^{-1/3})\text{-}(1\text{-}C)^{-2/3})$, $1/2(1\text{-}C)^{-1/2}$ and $1/3(1\text{-}C)^{-2/3}$ by the least squares method. From standard deviation of the fit and correlation coefficients, the first elimination reactions gave the best fits with the reaction type of $-\ln(1\text{-}C)$. The initial

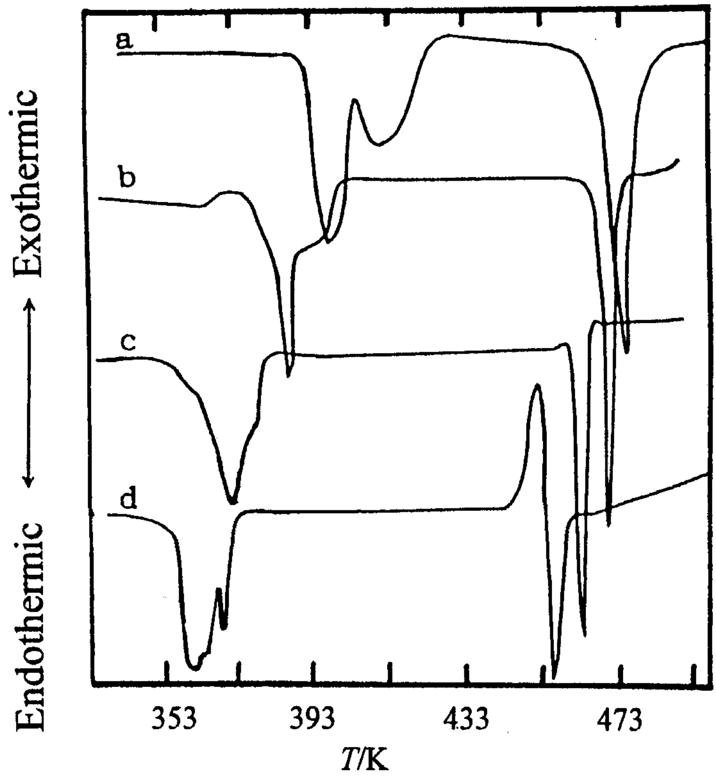

Figure 4 Scanning rate dependence of the DSC curve of the inclusion complex of acetophenone: a, 1200 K/h; b, 300 K/h; c, 60 K/h; d, 12 K/h.

elimination reaction of guest molecule from its inclusion complexes is the first order decay.

DSC and DTA curves obtained shows large dependence upon scanning rate as shown in Fig. 4 as an example. After the elimination of guest molecules, a exothermic peak was found just before the melting peak of the inclusion complex on DTA and DSC curves, however, there is no change on TG curves. The size of the exothermic peaks were not reproducible and depended on scanning rate as illustrated in Fig. 4. The temperature difference between the exothermic peak and next large endothermic peak of melting does not large enough to separate them by these scanning method. The exothermic peaks might be due to transition to more stable form before melting. There is no thermal anomaly in TG-DTA and DSC from the initial endothermic elimination peak of guest molecules to the exothermic peak. The host cholic acid keeping some vacancies which was obtained by release of guest molecules seems to be stable under ambient temperature.

Powder pattern of X-ray diffraction obtained with the "empty" host cholic acid was different from that obtained with the original, pure cholic acid. Therefore, new molecular assembly has been obtained by eliminating the guest molecules from the inclusion complexes of cholic acid with acetophenone, methanol and ethanol. The new molecular assembly of cholic acid are studying by solution calorimetry to obtain the enthalpies of formation of some new structure.

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