

COMPOSITION, PROPERTIES, STABILITY AND THERMAL DEHYDRATION OF CRYSTALLINE CAFFEINE HYDRATE

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ABSTRACT

It has been shown by gravimetric measurements that caffeine hydrate does not exist as a monohydrate but has a water content corresponding to a 5/6 or 4/5 hydrate. This result is supported by density determinations of crystals. The stability-point is found to be $\check{v}_D = 51.5 \pm 0.7$ °C. The enthalpy of dehydration is determined as well directly by DSC (6.8 ± 0.5 kJ mol⁻¹) as from the difference of integral enthalpies of solution of anhydrous caffeine and caffeine hydrate (7.06 ± 0.14 kJ mol⁻¹). The results and their consequences are discussed.

1. INTRODUCTION

A great portion of the caffeine used for the production of pharmaceuticals, beverages and foodstuffs is obtained by extraction from green coffee-beans to give decaffeinated coffee. There is now a tendency to replace the hitherto used solvents (e.g. CH₂Cl₂, dichlorethane) by dense, supercritical gases (e.g. CO₂, N₂O, C₂H₄) (1). In this case no potentially hazardous residues are left in the beans. Following the extraction process the caffeine is purified by fractional crystallization from aqueous solution.

Caffeine (1,3,7-trimethyl-2,6-dioxipurine) is long known to form a hydrate, in which the water is weakly bound by hydrogen bridges to the N-atoms in the 9-positions of different caffeine molecules in the crystal lattice. About the composition, stabi-

lity, properties, crystallization behavior, kinetics and energetics of dehydration etc. of caffeine hydrate information in the literature is scarce and even controversial. For improvements of the decaffeination process and the purification and use of caffeine, the knowledge of the cited properties became necessary. On the other hand, the behavior of caffeine hydrate, the hydrogen bonding, and the "base stacking" in its solutions deserve much interest on their own (2, 3, 4, 5).

2. BRIEF REVIEW OF THE PROPERTIES OF ANHYDROUS CAFFEINE

The thermophysical properties of anhydrous caffeine have been reported in a previous paper (6). Some of the data determined are listed below with respect to the properties of caffeine hydrate. The density at 25 °C was meanwhile found to be $1.454 \pm 0.01 \text{ g cm}^{-3}$. This is remarkably higher than the only literature value reported by PFAFF (7), who found 1.23 g cm^{-3} , which is certainly too low. The crystal structure of anhydrous caffeine is yet unknown. The following data have been determined by heat flux DSC (DuPont 990 Thermal Analyzer (8), Thermanalyse "MCB" (9)):

melting point $\nu_f/^\circ\text{C}$: 236.0 ± 0.2
 enthalpy of fusion $\Delta H_f/\text{kJ mol}^{-1}$: 21.6 ± 0.5 ((10): 22.4)
 entropy of fusion $\Delta S_f/\text{J K}^{-1} \text{ mol}^{-1}$: 42.4 ± 1.0
 transition point $\nu_t/^\circ\text{C}$: 141 ± 2
 enthalpy of transition $\Delta H_t/\text{kJ mol}^{-1}$: 4.1 ± 0.2
 entropy of transition $\Delta S_t/\text{J K}^{-1} \text{ mol}^{-1}$: 9.9 ± 0.5 .

3. COMPOSITION OF CAFFEINE HYDRATE

The caffeine hydrate was prepared by very slow crystallization from aqueous caffeine solutions, starting from a 99.95 mol-% material (DAB 7, HAG AG, Bremen), at a maximum temperature of 40 °C to avoid the production of anhydrous caffeine. The precipitate was filtered, centrifugated and stored under saturated vapour pressure conditions maintained by a saturated caffeine solution ("conditioning"). The purity, as determined by DSC, was 99.96 mol-%. This hydrate, called hydrate A, could only be prepared in needles of a maximum length of about 30 mm and a

corresponding diameter of about 0.1 mm, while crystals of a technical hydrate, obtained from HAG AG, had about the same length but a maximum diameter of about 3 mm and a purity of 99.8 mol-% at a slightly brownish colour.

The water content of caffeine hydrate was subject of some discussion in the literature. WATERS et al. (11), SUTOR (12) and GERDIL and MARSH (13) claimed a 5/6 or 4/5 hydrate, corresponding to a water content of about 7 weight per cent, while most of the literature and all the handbooks mention a monohydrate with 8.48 w.-% water. To clarify these differences, the water content of both hydrates was determined gravimetrically by drying samples of the conditioned hydrates in a desiccator at 80 °C over silicagel at atmospheric pressure to avoid any sublimation of the caffeine. It has been found that the water content of a hydrate prepared and stored under the conditions described was 6.95 ± 0.16 w.-% (hydrate A, 6 measurements) and 7.03 ± 0.04 w.-% (technical hydrate, as obtained, 40 measurements) resp. 7.10 ± 0.06 w.-% (technical hydrate, conditioned as hydrate A, 20 measurements). This is far from the composition of a monohydrate.

Density determinations by the floatation method, taking a mixture of carbon tetrachloride and toluene as floatation liquid, yielded densities of 1.415 ± 0.010 g cm⁻³ (hydrate A) resp. 1.418 ± 0.010 g cm⁻³ (technical hydrate). Due to some small mechanical impurities occluded in the technical hydrate, the value for hydrate A should be preferred. It should be mentioned that there were small differences in the densities of an ensemble of crystals, probably caused by some occlusion of solution. A density of 1.415 g cm⁻³ corresponds to a molecular weight of 207.7 ± 2.5 g mol⁻¹, calculated from the unit cell dimensions given by SUTOR (12), who herself found a density of 1.448 ± 0.004 g cm⁻³ (3 measurements), which results in a molecular weight of 212.4 ± 2.7 g mol⁻¹. The former value corresponds to a water content of about 6.5 ± 1.1 w.-%, the latter to a monohydrate, which however does not exist. This supports our value. The density of caffeine is thus slightly (2.7 %) higher than the density of its hydrate.

4. THE STABILITY-POINT

In the literature there is some confusion about the stability-point of caffeine hydrate. OECHLER (14) deduced it from solubility measurements and vapour pressure determinations over aqueous solutions to be about 44 °C, while KREMANN and JANETZKY (15) found 61 °C from solubility measurements. However, our present solubility determinations have shown that it is very difficult to obtain real equilibrium conditions in an aqueous caffeine solution at higher temperatures. This may be caused by the "base stacking" of the caffeine molecule at higher concentrations (formation of dimers, trimers etc. (5, 16)) and/or by the formation of a metastable form of caffeine (see below). This results in great uncertainties of the solubilities of caffeine in water above about 50 °C so that we have determined the stability-point of caffeine hydrate by prolonged "tempering" of samples of crystals at constant temperature and saturated water vapour pressure conditions (gas-tight capsules), followed by an analysis of the dehydration peak by DSC (see below). After a series of measurements at lower and higher temperatures, the hydrate was found to be stable at 51 °C for one week but decomposed (no dehydration peak by DSC) after three days at 52 °C; thus the stability point is 51.5 ± 0.7 °C. At low heating rates (< 0.5 K min^{-1}) the DSC peak used for analysis (Fig. 1) shows an incomplete recrystallization following the dehydration step, a fact, which has to be taken into account in the calculation of the dehydration enthalpy (see part 5.).

5. ENTHALPY OF DEHYDRATION

By calorimetry, the enthalpy of dehydration ΔH_D can either be determined directly, for example by DSC, or indirectly from the difference of the enthalpies of solution of caffeine and caffeine hydrate.

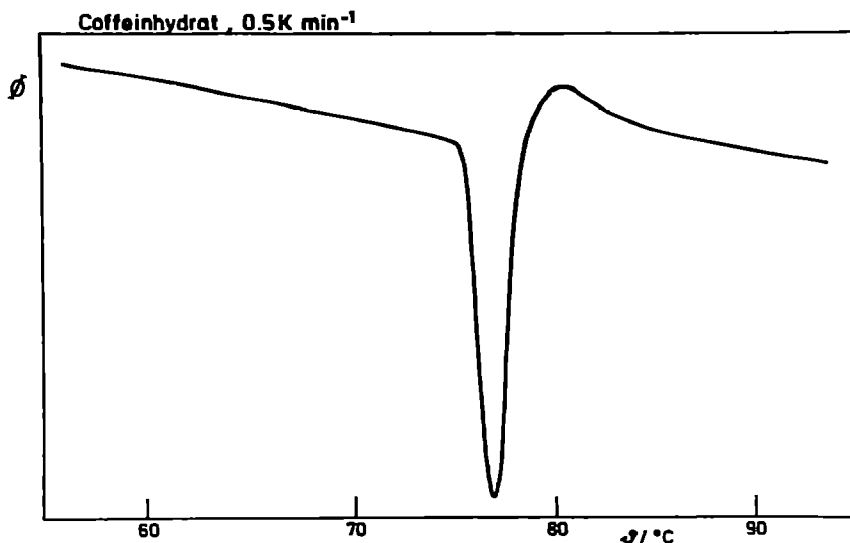


Fig. 1. DSC curve of caffeine hydrate at low heating rate showing dehydration peak followed by slow recrystallization

For the first method, gas-tight DSC capsules must be used to avoid vaporization of the produced water. Three corrections have to be applied in the calculation of the proper enthalpy of dehydration:

1. After the dehydration reaction, part of the water formed evaporates into the unoccupied volume of the DSC capsule (ΔH_V).
2. The rest of the water dissolves some caffeine to form a saturated solution (ΔH_{is}).
3. The dehydrated crystals first emerge in a metastable modification. Its enthalpy difference with respect to the stable β -caffeine ($\Delta \Delta H_t$) can be calculated from the measured enthalpy of transition of freshly dehydrated caffeine hydrate (dried under the same conditions as that used for the ΔH_D measurements), which is $\Delta \Delta H_t = 1.6 \pm 0.25 \text{ kJ mol}^{-1}$ lower than ΔH_t of β -caffeine.

Fig. 2 shows a typical curve for the dehydration reaction obtained with the MCB-calorimeter. The enthalpy of dehydration was calculated from the measured over-all enthalpy of reaction Δh by sub-

tracting the mentioned corrections

$$\Delta h_D = \Delta h - \Delta h_v - \Delta h_{is} - \Delta \Delta h_t. \quad (1)$$

The result is $\Delta H_D = 6.8 \pm 0.5 \text{ kJ mol}^{-1}$ (hydrate A) and $6.9 \pm 0.7 \text{ kJ mol}^{-1}$ (technical hydrate).

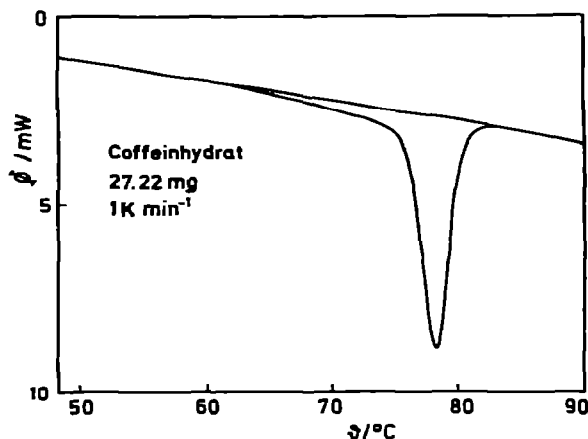


Fig. 2

DSC curve of the dehydration of caffeine hydrate.

In the present experiment:

$$\Delta h = 1.216 \text{ J}$$

$$\Delta h_v = 0.0144 \text{ J}$$

$$\Delta h_{is} = 0.0746 \text{ J}$$

$$\Delta H_D = 7.04 \text{ kJ mol}^{-1}$$

For the indirect determination of the dehydration enthalpy of caffeine hydrate exact values of the corresponding enthalpies of solution are necessary, but unfortunately the reported enthalpies of solution of caffeine seemed to be inaccurate (2, 4, 5), see table 1 below. Their differences are certainly greater than the uncertainties of the instruments used to obtain them, so that we had to redetermine the enthalpies of solution of both anhydrous and hydrated caffeine. An isoperibol solution calorimeter (LKB 8700-1) was used in the range of about 80 mg to 110 mg caffeine in 100,0 cm³ water at $25.00 \pm 0.02 \text{ }^\circ\text{C}$ ($\hat{=}$ concentration of about 0.005 mol l⁻¹ caffeine in water for both the hydrate and the anhydrous caffeine). The measurements were run in a compensating manner (see Fig. 3), so that no corrections for the heat loss of the calorimeter vessel (for example REGNAULT-PFAUNDLER) had to be applied. The anhydrous caffeine was used in its stable β -form, which was achieved by tempering dried caffeine hydrate for at least three days at 135 °C (6).

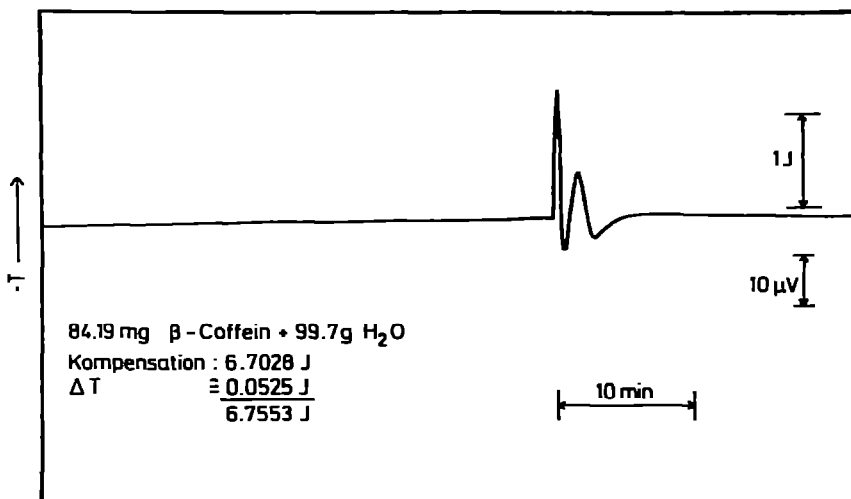


Fig. 3. Trace of an actual enthalpy of solution experiment. The endothermic heat of solution was almost completely compensated by appropriate electric heating.

The obtained values of $\Delta H_{is}^0 = 15.70 \pm 0.09 \text{ kJ mol}^{-1}$ (β -caffeine) resp. $22.76 \pm 0.10 \text{ kJ mol}^{-1}$ (hydrate A) are slightly higher than the literature values at the same temperature and concentration (2, 4, 5). In the case of anhydrous caffeine the difference may be due to the fact that caffeine obtained from crystallization in organic solvents and dried at about 80°C , as used in (2), has a higher enthalpy than β -caffeine (we have determined the difference to be about 0.6 kJ mol^{-1}) - a consequence of OSTWALD's step-rule. Without tempering sublimed caffeine, as used by STERN et al. (4) and CESÀRO et al. (5), has an enthalpy which is 1.3 kJ mol^{-1} higher than β -caffeine (both values obtained from a measurement of the corresponding enthalpy of transition). In the case of hydrate, the reason for the lower value of CESÀRO et al. (5) may be that they did not condition their crystals, but only wiped them with a filter paper. The much lower values of MATIGNON (17) are caused by the higher concentrations (0.04 mol l^{-1}) he used. At these concentrations the "base stacking" decreases the enthalpy of solution remarkably.

A calculation of the dehydration enthalpy from solubility determinations or from water vapour pressure measurements over saturated solutions of caffeine and caffeine hydrate according to

$$\Delta H_D = - R \Delta \left(\frac{d \ln c_s}{d \left(\frac{1}{T} \right)} \right)_{T_D} \quad (2)$$

or

$$\Delta H_D = - R \Delta \left(\frac{d \ln p_{H_2O}}{d \left(\frac{1}{T} \right)} \right)_{T_D} \quad (3)$$

is prevented by the wide scatter of the values reported in the literature resp. the inexact results of OECHLER (14). Table 1 shows the results of the calorimetric determinations together with data reported in the literature.

Table 1

stability-point	51.5 ± 0.7	isothermal "tempering"	(*)
$v_D^s / ^\circ C$	44	vapour pressure of saturated aqueous solutions;	
		solubility	(14)
	61	solubility	(15)
enthalpy of dehydration	6.8 ± 0.5	DSC	(*)
$\Delta H_D / kJ mol^{-1}$	7.06 ± 0.14	$\Delta \Delta H_{is}^o$ of anhydrous caffeine and caffeine hydrate	(*)
	6.7 ± 0.9	"	(5)
	7.2	"	(17)
enthalpy of solution	15.70 ± 0.09	β -caffeine	(*)
$\Delta H_{is}^o / kJ mol^{-1}$	14.35 ± 0.46	anhydrous caffeine (subl.)	(5)
	13.81 ± 0.14	" " "	(4)
	15.06 ± 0.50	" (crystals from benzene)	(2)
	22.76 ± 0.10	caffeine hydrate	(*)
	21.05 ± 0.71	" "	(5)

(*) this work

6. DISCUSSION AND OUTLOOK

Our dehydration measurements have unambiguously shown that caffeine hydrate does not exist as a monohydrate, as reported *inter alia* in (5, 14, 15, 17, 18, 19, 20), which would correspond to 8.48 w.-% water. Instead, the water content was found to be 6.95 ± 0.16 w.-%, which is close to a 4/5-hydrate (theoretical: 6.91 w.-%) or a 5/6-hydrate (theoretical: 7.18 w.-%). This is supported by previous findings of WATERS and BEAL (11), who obtained 6.95 w.-% and of TASSILY (21), who found 6.93 w.-%. However, TASSILY attributed this to experimental error and retained the monohydrate formula on the basis of his nitrogen analysis. The X-ray crystal structure determination by SUTOR (12) leads to about 0.8 mol of water per mol caffeine, with not very definite positions of the water molecules in the lattice (13). An investigation of the kinetics of the thermal dehydration of caffeine hydrate has been undertaken in our laboratory (22) and is planned to be followed by RAMAN spectroscopic measurements at different temperatures to study the hydrogen bonding.

Under its own water vapour pressure, caffeine hydrate is stable up to 51.5 ± 0.7 °C; at higher temperatures, anhydrous β -caffeine is the stable form (6). This is an important fact for the crystallization behavior of caffeine from aqueous solution, a procedure used in the purification of caffeine. It is often observed in practice that caffeine precipitates in tiny crystals, which are not easily to be filtered. The crystallization process is obviously complicated by the following facts: Above 51.5 °C, anhydrous caffeine precipitates, however not entirely as β -caffeine (which is the thermodynamically stable form below 141 °C), but partly in a metastable form. On further cooling below 51.5 °C, it is not anhydrous caffeine that is stable in aqueous solutions but caffeine hydrate. The crystallization is a slow process because nuclei have first to be formed either from solution or by hydration of the anhydrous crystals. If one starts below about 45 °C, crystallization leads to caffeine hydrate crystals without further complications.

Several authors have reported that caffeine solutions have an extreme tendency for supersaturation. In accordance, above about 50 °C the solubility data of different authors show wide diffe-

rences. Furthermore, the enthalpies of solution as measured by different authors do not accord (see above). Besides the existence of caffeine hydrate and of the modifications of caffeine, the "base stacking" in solution (which seems to be a slow process) may be responsible for some of the problems cited. We are currently measuring the enthalpy of solution as a function of temperature and concentration as well as the solubility over a wide range of temperatures. The results will be reported in the near future.

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