Table I. Standard Electrode Potentials of $Ni^{III,II}$-Peptide Complexes[a]

Ni(III) peptide	ΔmV[b]	E^0, V
Ni(H_{-2}glycylglycyl-L-histidine)	90	0.96
Ni(H_{-2}triglycine)	78	0.85
Ni(H_{-3}tetraglycinamide)	73	0.84
Ni(H_{-3}pentaglycine)$^-$	87	0.83
Ni(H_{-3}triglycinamide)	80	0.83
Ni(H_{-3}tetraglycine)$^-$	100	0.79

[a] Determined by cyclic voltammetry at 100 mV s^{-1} with a carbon paste working electrode, $[NiL]_T = 7.0 \times 10^{-4}$ M, 25 °C, $\mu = 0.1$ M $NaClO_4$, pH 9.3. [b] Peak to peak separation indicating the reversibility of the electrode reaction.

of trivalent nickel complexes increases with the number of deprotonated-peptide or deprotonated-amide nitrogen bonds. The proposed structure for the [$Ni^{III}(H_{-3}G_3a)$] complex has two deprotonated-peptide nitrogens, one deprotonated-amide nitrogen and one amine nitrogen bound to the metal. Complexes of tetraglycine, pentaglycine, tetraglycinamide, and triglycinamide have similar metal-nitrogen bonding and correspondingly similar electrode potentials. The glycylglycyl-L-histidine complex, which has two deprotonated-peptide nitrogens, an amine nitrogen, and an imidazole nitrogen coordinated, is thermodynamically and kinetically much less stable in the higher oxidation state of nickel than the preceding complexes. On the other hand the triglycine complex (with an amine, a carboxylate, and two deprotonated-peptides coordinated) has an electrode potential only slightly higher than the triply deprotonated-peptide complexes and $Ni^{III}(H_{-2}G_3)$ is slower to decompose in acid than is $Ni^{III}(H_{-3}G_3a)$. In general the relatively low electrode potentials of the Ni(III)-peptide complexes can be attributed to the strong electron-donor properties of the deprotonated-peptide nitrogen.

The $Ni^{III,II}$ potentials for G_4 and G_3a are 0.16 and 0.19 V greater than the corresponding $Cu^{III,II}$ potentials for these peptide complexes. Direct chemical evidence of the difference in potential is seen in the quantitative oxidation of $Cu^{II}(H_{-3}G_3a)^-$ to $Cu^{III}(H_{-3}G_3a)$ by $Ni^{III}(H_{-3}G_3a)$. The difference in potential can be attributed in part to the relative advantages in ligand field stabilization of d^8 vs. d^9 and d^7 electronic configurations in the square-planar or tetragonal environment of the peptide complexes.

Nickel(II) catalyzes the reaction of molecular oxygen with some oligopeptides in neutral solution.[9,10] The reaction produces small amounts of Ni(III)-peptides which are intermediates in the oxidation of the peptides. An autocatalytic pathway by which O_2 reacts to give Ni(III) species is under investigation in this laboratory. The relatively mild conditions under which the Ni(III) state is attained suggests that this unusual oxidation state of the metal may be important in other nickel(II) catalyzed reactions.

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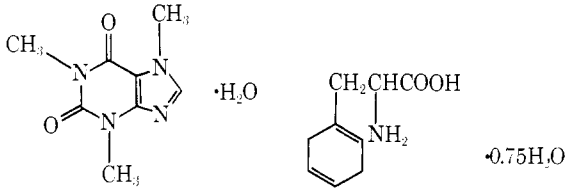
The Effect of Crystal Packing and Defects on Desolvation of Hydrate Crystals of Caffeine and L-(−)-1,4-Cyclohexadiene-1-alanine

Sir:

Numerous compounds are capable of existing in the solid state as hydrates and nonhydrated polymorphs.[1-12] Since the chemical[6] and physical properties[7] of crystal hydrates of drugs, e.g., caffeine[7] (I) and L-(−)-1,4-cyclohexadiene-1-alanine[6] (II) can differ markedly, crystal hydration may influence biological properties.[1,8,9] It is therefore important to understand what factors influence the solid state interconversion of such hydrates with their anhydrous forms.



I II

A typical crystal of caffeine hydrate (grown by slow evaporation of a water solution) and its anisotropic behavior upon dehydration is shown in Figure 1 (Ia through Id). The water

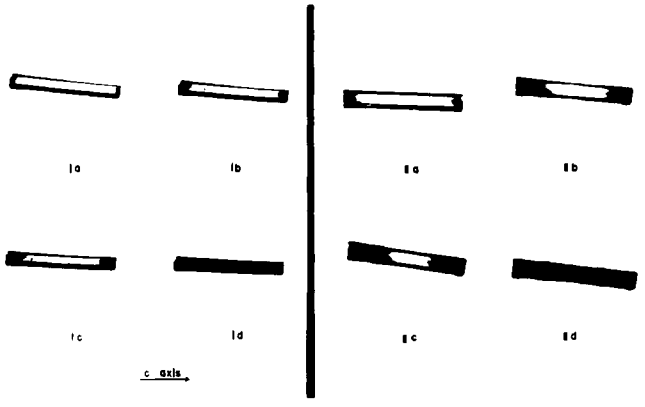


Figure 1. Behavior of a crystal (0.9 × 0.17 mm) of caffeine monohydrate (Ia through Id) in air at room temperature after both ends were cut off using a razor blade: (a) immediately after cutting; (b) after 4 h at room temperature; (c) after 24 h at room temperature; and (d) after 72 h at room temperature. Precession photography showed that the *c* axis paralleled the elongated direction of the crystal (horizontal axis in the photograph) and that the *a* axis was the vertical axis in the photograph. The nature of the crystals prevented goniometric determination of the Miller indices of the crystal faces but the precession studies showed that the end face approximated the (001) face while the top face approximated the (100) face. Photographs IIa through IId show the behavior of a crystal (1 × 0.2 mm) of L-(−)-1,4-cyclohexadiene-1-alanine·0.75H_2O in air at room temperature after both ends were cut off with a razor blade: (a) after 0.5 h; (b) after 2 h; (c) after 3 h, and (d) after 5 h.

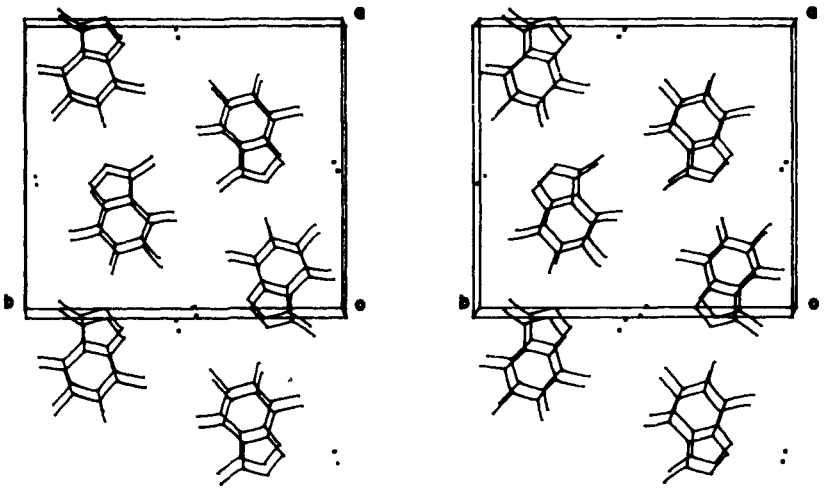


Figure 2. Stereopair drawing of the crystal packing of caffeine monohydrate viewed perpendicular to the (001) face.[14] The oxygen atoms of the water molecules are designated by dots.

molecules appear to preferentially exit from the ends of the crystals which were removed by cutting with a razor blade. In the initial stages of the reaction the dehydration moves in a front from the ends toward the center.[10] Crystals without the ends removed and crystals cut parallel to the elongated direction of the crystal (c axis) still preferentially desolvated from the ends.

Figure 2 is a stereoscopic view of the crystal packing of caffeine looking down the long direction (*c* axis) of the crystal. There are tunnels of water molecules approximately parallel to this axis.

The anisotropic behavior is explained by the preferential escape of the water molecules along these tunnels. Desolvation from other crystal directions would require the water molecules to penetrate the somewhat closely packed layers of nonpolar groups in the other two crystallographic directions. This explanation is given added support because of its similarity to the explanations of the anisotropic behavior of benzoic acid crystals upon reactions with ammonia gas.[13]

The behavior of crystals of the hydrate of L-(−)-1,4-cyclohexadiene-1-alanine (II) prepared according to literature routes was even more striking. Crystals of the hydrate were prepared by slow evaporation of an 80% ethanol or methanol-ethyl acetate solution under a stream of nitrogen gas. Figure 1 (IIa through IId) shows the behavior of a crystal of II which was cut on both ends. Loss of water of crystallization proceeded toward the center in fronts starting from the ends in marked similarity to caffeine. However, the crystals of II were much more sensitive to defects than caffeine hydrate crystals. Nearly perfect crystals of dihydrophenylalanine hydrate (II) were much more stable than those with observable defects and cutting the ends off provided defects which led to the anisotropic behavior of these crystals. If only one end of a crystal was removed then dehydration proceeded in a front from that end toward the other. A stream of nitrogen gas caused a five- to tenfold increase in the rate of dehydration.

The rapid dehydration of II has thus far prevented the determination of its crystal structure since the diffraction intensity of the opaque crystals was very low.

At room temperature in air, dehydration appears to be much faster than the solid state dehydrogenation of dihydrophenylalanine hydrate (II). Analysis of a typical batch of opaque crystals showed that in 2 h only 2.76% phenylalanine was present, in 5 days 8.3%, and in 10 days only 16.73%. This is consistent with the suggestions of Ressler that water loss preceded the dehydrogenation.[6]

These studies suggest that desolvation reactions are influenced by both crystal packing and crystal defects. The influence of crystal packing on these reactions is similar to the influence of packing on solid + gas → solid reactions, particularly those of acids and anhydrides with ammonia.[13] The influence of defects on the reaction of dihydrophenylalanine hydrate is striking and is related to the phase transformation of *p*-dichlorobenzene where mechanically produced defects induced the solid state transformation.[15]

In conclusion, it is interesting to compare the behavior of the hydrate crystals discussed to clathrates.[16] In clathrates the solvent molecules are entrapped in a cage and the crystals are often quite stable. On the other hand in these hydrate crystals the solvent molecules are not entrapped and defects accelerate the desolvation along the water tunnel direction.

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