

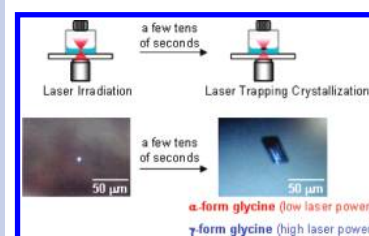
Control of Crystal Polymorph of Glycine by Photon Pressure of a Focused Continuous Wave Near-Infrared Laser Beam

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ABSTRACT Crystal polymorph of glycine is controlled by tuning the power of a linearly polarized continuous wave 1064-nm laser beam. Upon focusing the beam to the air/solution interface of a supersaturated glycine/D₂O solution, its single crystal is spatiotemporally formed at a focal spot within a few seconds to a few tens of seconds. Fourier transform infrared measurement and single-crystal X-ray crystallographic analysis of the fabricated single crystal reveal that two polymorphs of α - and γ -forms are prepared depending on the laser power. The probability of γ -form preparation, which is not available under ambient conditions, arises up to 50% at 1.3 W laser power after an objective lens. The mechanism of the polymorph control is discussed in view of both photon pressure and local temperature elevation due to laser irradiation at the focal spot.

SECTION Nanoparticles and Nanostructures



Control of crystal polymorphs has received much attention in many fields of molecular, material, biological, and chemical sciences, since crystal polymorphs show different physical and chemical properties such as melting point, solubility, optical property, and so on.^{1–4} Glycine has been employed as a representative compound in many studies on polymorphic crystallization, and three polymorphs are known.^{5–10} α -Form is prepared by the spontaneous crystallization from neutral aqueous solution, although it is not the most stable polymorph among those forms at ordinary temperatures and pressures.^{5,10} β -Form is present just under special conditions, and rapidly transforms into the α -one in air or/and water.^{11,12} γ -Form is prepared only under comparatively severe experimental conditions (e.g., high pressure, high acidic/basic, or high supersaturated) or by adding some additive salts into the aqueous solution, despite the fact that it is the most thermodynamically stable among the three polymorphs.^{6,7,13–17}

As a crystallization method by laser irradiation, Garetz and co-workers demonstrated that nanosecond-pulsed laser irradiation of supersaturated solutions of amino acids, urea, proteins, and so on leads to their crystallization. They called this phenomenon nonphotochemical laser-induced nucleation (NPLIN),^{18,19} and they also succeeded in controlling glycine polymorphs of α - and γ -forms by switching the polarization of the laser beam.²⁰ On the other hand, just by utilizing photon pressure of a focused continuous wave (CW) near-infrared (NIR) laser beam,²¹ we have recently succeeded in glycine crystallization spatiotemporally in

supersaturated D₂O solution, and have called this phenomenon “laser trapping crystallization”. In this laser trapping crystallization, the liquid-like clusters of glycine formed in the supersaturated solution are gathered in a focal point under the photon pressure, and the local association of the clusters is enhanced. The molecules in the association should be reoriented and reorganized, eventually leading to the nucleation. Separately, we have reported that the growth rate and its direction of a spontaneously produced glycine crystal in D₂O is arbitrarily controlled by trapping the glycine clusters near the crystal. This means high concentration regions of the clusters are formed.²² In this paper, we present the first study on crystal polymorph control by photon pressure of a focused CW NIR laser beam. Except under severe conditions, glycine tends to crystallize to the γ -form from the high supersaturated solution via quite slow evaporation or cooling,¹⁷ so that the high supersaturated spot of the molecules produced by photon pressure at high laser power may lead to the γ -form preparation.

Figure 1 shows a schematic illustration of the optical trapping system in this experiment. In order to avoid temperature elevation during laser irradiation, D₂O was used as a solvent. Upon focusing a linearly polarized CW 1064-nm laser beam at the air/solution interface of the supersaturated

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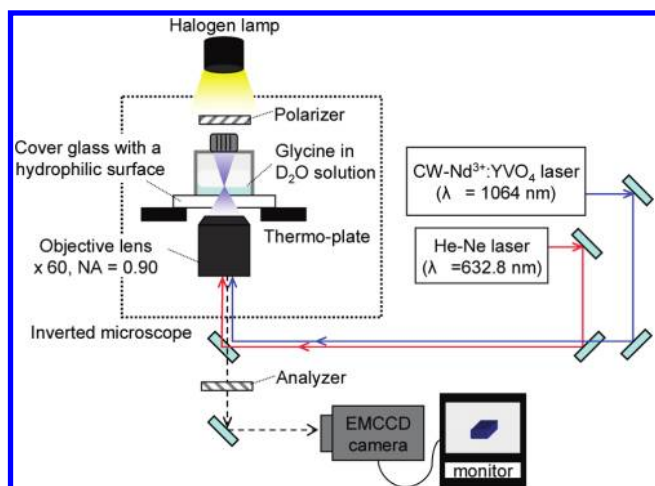


Figure 1. A schematic illustration of the optical trapping system of the photon pressure-induced crystallization from a supersaturated glycine/D₂O solution.

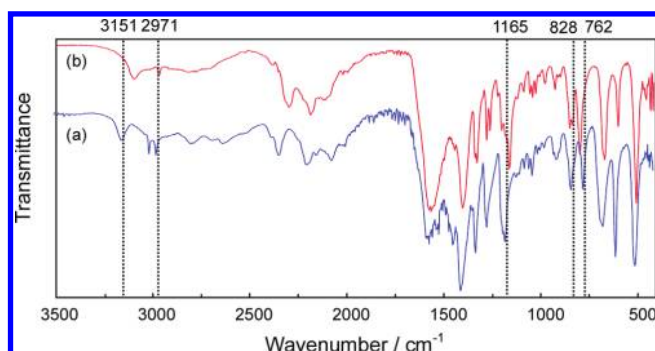


Figure 2. FTIR spectra of glycine crystals prepared by applying the photon pressure of a focused CW NIR laser beam. Obtained spectra "a" and "b" are assigned to α - and γ -forms of glycine-d₃, respectively.

glycine/D₂O solution, one crystal was prepared and observed at the focal spot within a few tens of seconds as in a previous report.²¹ The crystallization was observed in all samples that we tried in this experiment. After one crystal grew up to a few millimeters in size by aging for 3 h in the solution, it was taken out from the sample bottle and examined by Fourier transform infrared (FTIR) measurement. Always only one large crystal was prepared in the center of the bottom near the focal point. By measuring the FTIR spectrum of each large crystal, we found that all of the obtained spectra can be classified into two types (Figure 2), and no mixture of these two spectra was formed.

The H atoms of an amino group of glycine in heavy water are replaced by D atoms, so that the vibrational frequencies of N-deuterated glycine (ND₃⁺CH₂COO⁻, glycine-d₃) are important, which was reported by Suzuki et al., in 1963.²³ They pointed out that the FTIR spectrum of α -form showed the sharp peaks of CH₂ stretching around 3070–2940 cm⁻¹, whereas that of glycine appeared to be a broad region. In addition, the peaks shifted from the regions at 1527–1502 and 1131–1111 to 1188–1166 and 822–763 cm⁻¹,

respectively, which showed the change in vibrational mode of NH₃ to ND₃ deformation and rocking, respectively. Taking this into consideration, Figure 2a shows sharp peaks at 3151–2971, 1180–1165, and 828–762 cm⁻¹, all of which are consistent with the previous reports. It implies that glycine was changed into glycine-d₃ in D₂O, and its polymorph was ascribed to the α -form. In addition, the crystal polymorph was also confirmed by single-crystal X-ray crystallographic analysis (see a further discussion below). Indeed, the glycine crystal spontaneously obtained from the supersaturated glycine/D₂O solution after 1–2 days also showed the same FTIR bands as those in Figure 2a.

It was reported that, when keeping α -form glycine crystal in the solution for a long period, its polymorph gradually changes to the γ -form, which is the most thermodynamically stable phase, namely, solution-mediated phase transformation.^{10,14} Therefore, in order to investigate whether the transformation occurred while the formed crystal was kept in the solution, we measured temporal changes of the FTIR spectrum of the α -form crystal spontaneously formed in the solution. We found that no change in the FTIR spectrum was identified until 4 days, while after that it changed to a spectrum maintaining characteristics of the α -form and having some partial peak shifts (see Figure S1 in Supporting Information). This indicates that the crystal polymorph started transforming from the α -form to the γ -one after 4 days. On the basis of the results and carefully considering our experimental conditions, it is considered that the solution-mediated transformation did not take place within 3 h before FTIR measurement. Furthermore, if the transformation had occurred within such a short time, we would have obtained only the γ -form. After aging for 1 week, the transformation from the α -form to the γ -one was almost finished, giving the same FTIR spectrum as shown in Figure 2b. In other words, Figure 2b, which shows a low frequency shifted CH₂ stretching at 3094–2971, ND₃ deformation at 1167–1153, and ND₃ rocking at 824–787 cm⁻¹, can be ascribed to the characteristic peak of the γ -form of glycine-d₃. Consequently, we conclude that both the α - and γ -forms were produced by the photon pressure, not via the solution-mediated transformation.

To clarify the precise structures of two polymorphs, single-crystal X-ray crystallographic analysis was carried out. The results revealed that two polymorphs of glycine prepared by the photon pressure were certainly ascribed to the α - and γ -forms, respectively, which are consistent with the results of FTIR measurement as described above. The crystal structure of the α -form is monoclinic, and belongs to space group $P2_1/n$. For the γ -form, the crystal structure is trigonal and has a chiral space group ($P3_1$). The crystal parameters of the two polymorphs of deuterated glycine are quite similar to those prepared from H₂O.²⁴

As described above,¹⁷ glycine tends to crystallize to the γ -form from the high supersaturated solution. As laser power increases, the concentration of the liquid-like clusters in the focal spot should be higher due to deeper optical potential. Therefore, in order to investigate how the laser power affects the probability of γ -form preparation, FTIR measurement was carried out for the crystals prepared with the power varying

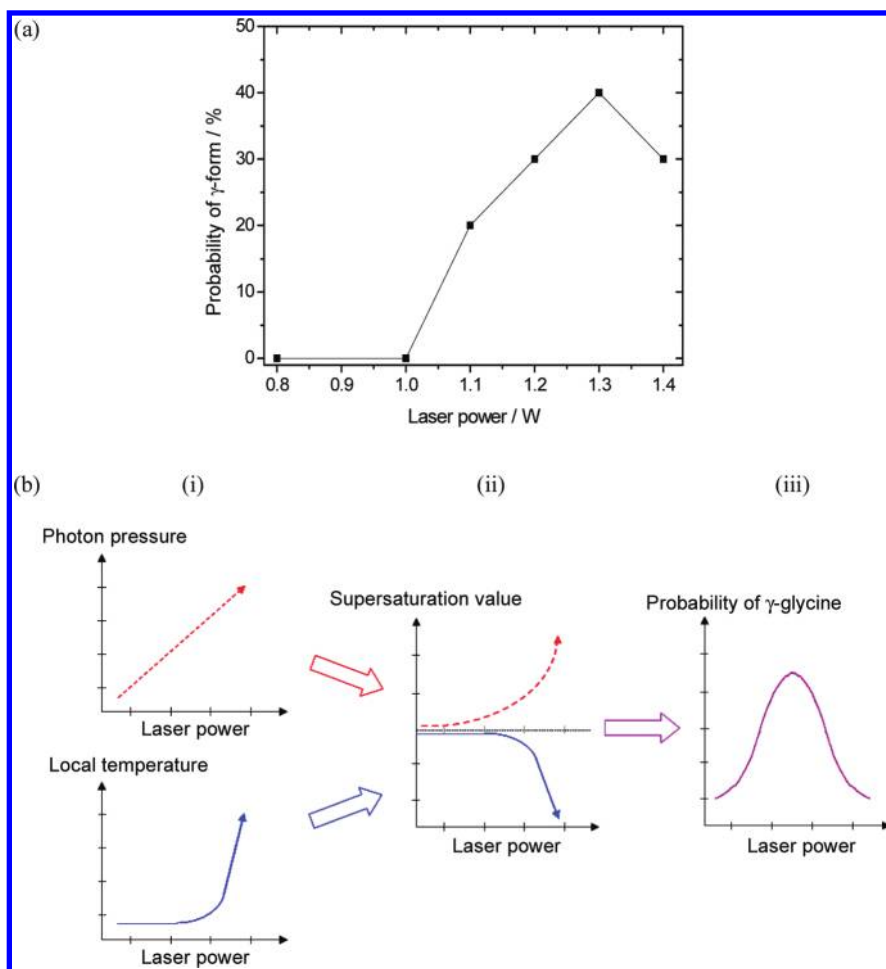


Figure 3. (a) Laser power dependence of the probability of γ -glycine preparation induced by the photon pressure of the linearly polarized CW NIR laser beam and (b) a bell-shaped curve of the multiplication of two effects: photon pressure and local temperature elevation.

from 0.8 to 1.4 W. The probability was investigated for 10 samples at each laser power, and the results are shown in Figure 3a. In the case of the laser power lower than 1.0 W, only the α -form was obtained. While the laser power became higher, the probability gradually became higher and reached a maximum of 40 % at 1.3 W. However, it decreased to 20 % at 1.4 W, which is the maximum laser power in this experiment. Why the probability does not reach to 100 % is explained as follows: The concentration of glycine liquid-like clusters in the focal spot increases from time to time by laser irradiation. At first, a certain supersaturation, where the nucleation to α -form occurs as in bulk solution, is attained. As the nucleation is a statistical phenomenon, the concentration sometimes increases faster before the α -form nucleus is produced and possibly comes to a higher region, where the γ -form can be nucleated. Therefore, a 40 % probability of γ -glycine was obtained under the present conditions.

The generation of γ -form can possibly be explained by two reciprocal laser power-dependent effects: photon pressure and local temperature elevation in the focal spot. As illustrated in Figure 3b, the interaction of a focused laser beam and the liquid-like cluster induces photon pressure, the force of which is proportional to the laser power. Simultaneously, the laser

beam causes a local temperature elevation mainly due to the absorption of a 1064 nm photon by the glycine molecule itself, since it has a larger absorption coefficient at 1064 nm than D_2O (Figure 3b(i)). The molecular concentration of glycine liquid-like clusters increases with time, and larger associates receive deeper trapping potential. Thus, nonlinear increase of glycine clusters is realized. These glycine clusters are responsible for laser-induced heating. Thus, the temperature elevation is nonlinearly enhanced with the laser power. The elevation becomes relatively apparent at the high laser power region, and overcomes the dissipation.

Next, we consider the changes of the supersaturation value with respect to the photon pressure and the local temperature elevation, as illustrated in Figure 3b(ii), as the polymorph of glycine depends on the supersaturation degree on the nucleation as described above.¹⁷ Since the photon pressure is enhanced more as a result of the gathering of the liquid-like clusters, the supersaturation value in the focal spot nonlinearly increases with the laser power, leading to a higher probability of γ -glycine formation. On the contrary, the supersaturation value is reduced by the local temperature elevation, and its tendency suddenly becomes large above a certain laser power where the thermal dissipation is overcome by

input laser power. Thus, the probability of γ -form preparation is considered to be represented by the multiplication of these two factors; consequently, a bell-shaped curve as illustrated in Figure 3b(iii) is obtained. This explanation supports the present result showing in Figure 3a.

In summary, we have succeeded in the crystallization of glycine in D_2O by photon pressure of a focused CW NIR laser beam, and in controlling the crystal polymorph just by changing the laser power. Interestingly, only one crystal with the polymorph control was spatiotemporally obtained just at the focal spot within a few tens of seconds. The control mechanism was proposed in view of the change of supersaturation degree in the focal spot, and discussed on the basis of photon pressure and temperature elevation depending on the laser power. In spite of the fact that the spontaneous crystallization of glycine is controlled kinetically rather than thermodynamically, giving the α -form,^{5,10} we have found that the γ -form glycine crystal was achieved by high photon pressure. The present work clearly shows that photon pressure enables us to control the polymorph. Other parameters probably reflecting the crystal polymorph, e.g., concentration, temperature, solvent, laser polarization, and so on, are under investigation and will be reported in the near future.

EXPERIMENTAL METHODS

Supersaturated glycine/ D_2O solutions (ca. 3.6 M) were prepared by dissolving glycine (0.3 g) in D_2O (1.0 g) at 60 °C with vigorous shaking for 3 h, and were cooled down slowly to room temperature. The samples with no spontaneous crystallization after half-a-day were used for experiments. A 15 μ L portion of the solution was dropped into a handmade sample bottle, which has a glass bottom with a highly hydrophilic surface and a spigot. The spigot was immediately and firmly closed to avoid solvent evaporation. Incidentally, no spontaneous crystallization was observed for at least 1 month under these experimental conditions. The thin film of the solution was instantly formed in the bottle, which was kept at 23 °C by a thermo plate, while the thickness was estimated to be about 150 μ m. A linearly polarized laser beam with 1064 nm from a CW Nd³⁺:YVO₄ laser beam (Spectra Physics, J20-BL-106C) was used as an optical trapping light source. It was introduced into an inverted microscope and tightly focused at the air/solution interface via an objective lens (60 \times magnification, NA 0.90). The focal position was confirmed by a He–Ne laser (Coherent, 6069DU), which was coaxial to a trapping laser path. The laser power after the objective lens was varied from 0.8 to 1.4 W by using a half wave plate and a polarized beam splitter. Crossed Nicols images of formed crystals were recorded by an EMCCD video camera (Flovel, ADT-40C). X-ray diffraction data were collected on a Rigaku RAXIS RAPID diffractometer with a two-dimensional (2D) area detector using graphite-monochromatized Cu K α radiation ($\lambda = 1.54178$ Å). Lattice parameters were obtained by a least-squares analysis from reflections for three oscillation images. Direct methods (SIR2004)²⁵ were used for the structure solutions. All calculations were performed for the observed reflections [$I > 2\sigma(I)$] by the program CrystalStructure crystallographic software

packages²⁶ except for refinement, which was performed using SHELXL-97.²⁷ All non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms were placed in idealized positions and refined as rigid atoms with the relative isotropic displacement parameters. Details of the X-ray crystal structure analyses of the α - and γ -forms are compiled in Table S1 in the Supporting Information.

SUPPORTING INFORMATION AVAILABLE Details of the X-ray crystal structure analyses of the α - and γ -forms, and FTIR spectra of spontaneous glycine crystals after being left in the solution for 2, 5, and 8 days. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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