First Observation of Precursory Structural Changes of Aliphatic Parts in the α-γ Polymorphic Transition of DL-Norleucine by Temperature-Scanning Time-Resolved FT-IR Spectroscopy

Masashi Sonoyama,* Hirofumi Yajima,† Tatsuhiko Nakano,†† Masayuki Matsumoto,†††
Itaru Tsukushi,†††† and Tadahiro Ishii†
Department of Biotechnology, Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588,
†*Department of Applied Chemistry, Science University of Tokyo, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601*
††*Nippon Bio-Rad Laboratories, 5-7-18 Higashi-Nippori, Arakawa-ku, Tokyo 116-0014*
†††*Shobi Junior College, 655 Matsubara, Kawagoe, Saitama 350-1153*
††††*Department of Physics, Chiba Institute of Technology, 2-1-1 Shibazono, Narashino, Chiba 275-0023*

(Received February 4, 2000; CL-000124)

Polymorphic transition of DL-norleucine from the α-form to the γ-form was investigated with temperature-scanning time-resolved FT-IR spectroscopy. The dynamic FT-IR measurements revealed the precursory structural changes in the aliphatic parts prior to the main overall polymorphic transition.

Polymorphism of amino acids has been widely investigated by X-ray diffraction, differential scanning calorimetry (D.S.C.), solid-state nuclear magnetic resonance and vibrational spectroscopy for several decades. It was recently reported from D.S.C. measurements by Matsumoto et al. that aliphatic α-amino acids with a normal alkyl side chain of the even carbon number, such as DL-2-amino butanoic acid (DL-ABA) and DL-norleucine (DL-NL), have a very interesting polymorphic transformation upon heating.[1] (1) The α-γ transition for DL-NL is reversible and very drastic, while the A-B transformation for DL-ABA, irreversible and gradual, (2) transition temperature (Tt) is impervious to water content (WC) for DL-NL. In the case of DL-ABA, on the other hand, Tt responds to WC strongly.

There remain, however, several questions to be examined about the crystalline phase transition of the two amino acids. One is that what is responsible for the differences between them in their transformation as pointed out above. Detailed structural changes in the process are also an important point to be studied for understanding the polymorphism. To address the questions, FT-IR spectroscopy with temperature-scanning was employed for the investigation of structural changes of DL-NL in the polymorphic transition in the present study.

DL-NL was purchased from Sigma Chem. Co. and recrystallization from water was performed three times for purification. Rapid-scan time-resolved infrared spectra of DL-NL under the crystalline phase transition were measured with a Bio-Rad FTS-575C FT-IR spectrometer equipped with an infrared microscope UMA 500. A single scan was performed for each spectrum at the spectral resolution of 4 cm^{-1} and with the time resolution of 190 ms. The temperature of the sample was continuously elevated at the heating rate of 5 °C/min with a Mettler FP82HT temperature controller to carry out comparative studies with the previous D.S.C. results by Matsumoto et al.[1] A series of spectra was collected at the interval of 1.6×10^{-2} °C under the conditions.

Infrared spectrum at 30 °C (data not shown) is almost identical to the previous results by Tsuboi et al.[2] and Matsumoto et al.[3], indicating that the recrystallized DL-NL used in this study adopts the α-form. Representative time-resolved IR spectra in the fingerprint region at the temperature of 117-120 °C are shown in Figure 1. No significant spectral changes were observed upon heating to 117 °C except in several spectral regions associated with the aliphatic groups. This indicates that overall drastic structural changes are not induced below 117 °C, as reported in the previous calorimetric studies by Matsumoto et al.[1,3,4] The minute spectral changes in the aliphatic vibrational modes will be discussed in detail elsewhere with the results of experiments on deuterated compounds and normal mode analyses for several plausible conformational isomers of DL-NL.

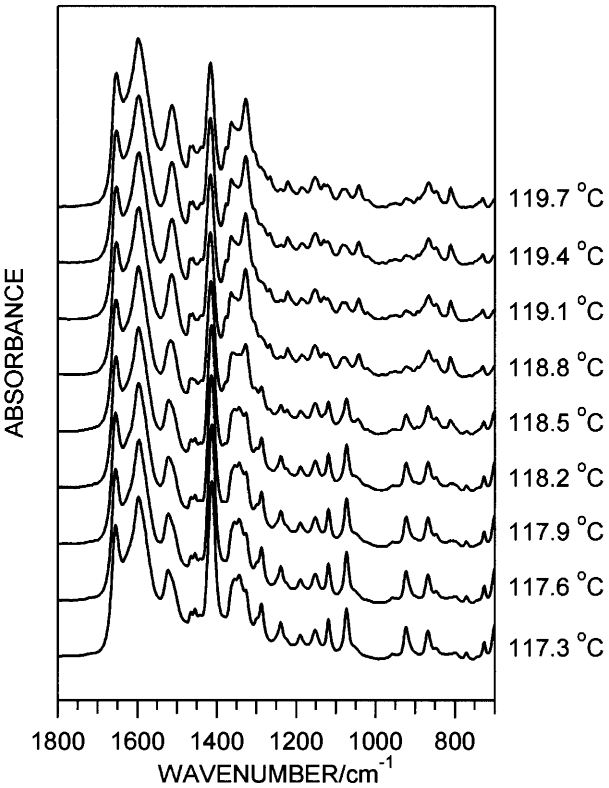

Figure 1. Infrared spectral changes of DL-NL in the temperature range of 117.3-119.7 °C.

Upon further elevation of temperature up to 118 ºC, drastic spectral changes occur in many spectral regions. Notable bands that significantly decrease in absorbance are the COO^- symmetric stretching band at 1414 cm^{-1}, the CH bending band at 1340 cm^{-1}, NH_3^+ rocking mode at 1118 cm^{-1} and the coupling mode of the CH_2 rocking and the C-C stretching at 1072 cm^{-1}, and the COO^- bending band at 810 cm^{-1}. These bands are characteristic of the α-form. The bands at 1325, 1042 and 923 cm^{-1}, on the other hand, appear upon the α-γ crystalline transition. The peaks at 1325 and 1042 cm^{-1} correspond to the ones at 1340, 1072 cm^{-1} observed in the spectrum of DL-NL with the α-form, respectively. The feature at 923 cm^{-1} is assignable to the CH_2 rocking mode for the γ-form. The bands corresponding to the counter crystalline form are not clearly identified for the ones at 923 and 810 cm^{-1} at present. The six representative bands mentioned above are summarized in Table 1. Above ~119 ºC, however, the spectra were almost identical with each other, indicating that the α-γ structural transformation of DL-NL occurs as in the narrow temperature range as around 1 ºC, which is in good accordance with the previous D.S.C. results.[1,3,4] When the sample is cooled down to room temperature, its spectrum is identical with the one before heating, showing that the α-γ polymorphic transformation of DL-NL is reversible.

Table 1. Frequencies and assignments of representative infrared bands of DL-NL with the α- and γ- forms

Frequency/cm^{-1}		Assignment
α-form	γ-form	
1411	1422	COO^- sym.[a] str.[b]
1340	1324	CH bend.[c]
1116	1131	NH_3^+ bend.[c]
1072	1042	C-C str. CH_2 rock.[d]
920	–	CH_2 rock[d]
–	810	COO^- bend.[c]

[a]sym.; symmetric. [b]str.; stretching. [c]bend.; bending. [d]rock.; rocking.

In order to examine polymorphic transition of DL-NL in more detail, absorbance changes were calculated for vibrational modes that significantly change their intensities. The results for the six representative bands are shown in Figure 2. Drastic absorbance changes are observed at ~118 ºC for many bands including the representative bands. The very sharp structural transition revealed by FT-IR spectroscopy is in good agreement with the previous D.S.C. results.[1,3,4] It should be noted that the main transition occurs in the very narrow temperature range for DL-NL. When the time-resolved spectra were measured at the time resolution higher than several hundreds millisecond, however, gradual absorbance changes prior to the main spectral changes were clearly observed for the vibrational modes due to the aliphatic parts of the molecule, while the bands due to the NH_3^+ and COO^- groups, that have strong inter- and intra-layer interaction through hydrogen bonds, show no clear absorbance changes prior to the main transition. The first observation of the precursory structural changes in the aliphatic region was achieved by the moderate high time-resolved FT-IR spectroscopy. This indicates that structural changes in the aliphatic group are induced prior to those in the whole molecule including the polar region. The differences in absorbance changes between the aliphatic groups and the polar ones suggest that the gradual structural changes in the aliphatic region trigger the overall polymorphic transition.

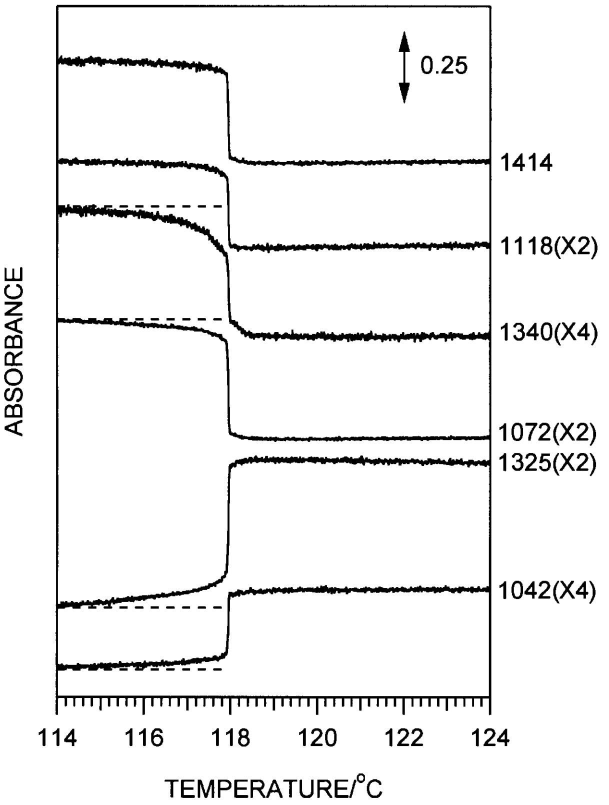

Figure 2. Absorbance changes of the six representative infrared bands of DL-NL in the temperature range of 114-124 ºC.

References

1 M. Matsumoto, H. Yajima, Y. Tezuka, T. Ishii, K. Takahashi, and A. Asai, *Chem. Lett.*, **1997**, 193.

2 M. Matsumoto and K. S. Kunihisa, *Chem. Lett.*, **1984**, 1279.

3 M. Matsumoto, H. Yajima, and T. Handa, *Bull. Chem. Soc. Jpn.*, **59**, 3803 (1986).

4 M. Tsuboi, Y. Iidaka, S. Suzuki, and S. Mizushima, *Bull. Chem. Soc.*, Jpn., **32**, 529(1959).