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Pantolactone as a Plastic Crystal

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D-Pantolactone crystals showed anomalous thermal behavior, that is, two endothermic peaks (62.0 and 91.6 °C) were observed in the differential scanning calorimetry curves. The entropy change of the first transition was calculated as $44.4\,\mathrm{JK^{-1}\,mol^{-1}}$ and that of the second transition was $9.20\,\mathrm{JK^{-1}\,mol^{-1}}$. The powder X-ray diffraction patterns of D-pantolactone differed significantly before and after the transition (62.0 °C) and only one sharp peak at $2\theta = 17.4°$ was observed at 75 °C. At 75 °C, carbon-13 nuclear magnetic resonance chemical shifts of D-pantolactone were clearly observed by the pulse Fourier-transform technique.

It was concluded that D- and L-pantolactone showed a stable plastic crystal phase between 62.0 and 91.6 °C, and that DL-pantolactone is in a plastic crystal phase at room temperature.

Keywords——plastic crystal; phase transition; mesophase; NMR; X-ray diffraction; thermal analysis

Phase transitions of organic crystals include polymorphic transition,[1] liquid crystal[2] and plastic crystal transition,[3] and glass transition,[4] as well as fusion and solidification.

Pantolactone (dihydro-3-hydroxy-4*H*-dimethyl-2(3*H*)-furanone), a metabolite of pantothenic acid in the liver, is an optically active compound with unusual thermal behavior. In the present study, its anomalous thermal behaviour was investigated by using differential scanning calorimetry (DSC), powder X-ray diffraction and nuclear magnetic resonance (NMR) spectroscopy.

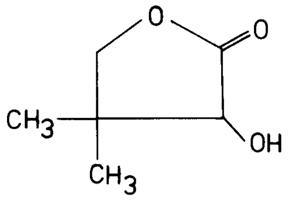

Chart 1

Experimental

Materials——D-Pantolactone (Tokyo Kasei Kogyo Co., Ltd.), L-pantolactone (Nakarai Chemicals Ltd.) and DL-pantolactone (Nakarai Chemicals Ltd.) were used without further purification.

Powder X-Ray Diffraction——Powder X-ray diffraction patterns were measured using a Phillips DW 1730/10 diffractometer equipped with a heating apparatus. The temperature dependence of the powder patterns was measured between 25 and 100 °C. The operating conditions were as follows: X-ray generator ($\mathrm{Cu}K_\alpha$, Ni-filtered, 40 kV, 20 mA) with a scintillation counter.

Differential Scanning Calorimetry——A Perkin Elmer DSC 1-B differential scanning calorimeter was used. The measurements were done using the sample pan for the liquid sample at a scanning speed of 8 °C/min under N_2 gas flow.

Infrared (IR) Absorption Spectroscopy——A Hitachi 295 IR spectrophotometer was used. The measurements were made by the KBr disk method. The temperature dependence of IR was measured between 25 and 100 °C.

NMR Measurement——The ^{13}C-NMR spectra of solid samples were observed on a JEOL FX-200 spectrometer. The temperature-dependent NMR spectra were measured between 25 and 100 °C.

Results and Discussion

Thermal Analysis of Pantolactone

Figure 1 shows DSC curves of D- and DL-pantolactone crystals. D-Pantolactone showed two endothermic peaks at 62.0 and 91.6 °C (curve A). From the observation of D-pantolactone crystals under a microscope, it was seen that a solid phase was apparently maintained after the first transition at 62.0 °C. The peak at 91.6 °C was due to the melting of D-pantolactone crystals. The entropy changes at the transition point (ΔS_t) and at the melting point (ΔS_m) were calculated from the DSC peak areas as 44.4 and 9.20 $JK^{-1} mol^{-1}$ respectively. Curve B shows the DSC rerun of a D-pantolactone sample which was preheated to 110 °C and then cooled to room temperature in the DSC cell before DSC measurement. The endothermic peak at 62.0 °C originally observed in curve A was no longer seen. Similar thermal behavior was observed with L-pantolactone. DL-Pantolactone showed an endothermic peak corresponding to melting at 78.1 °C, the entropy change of which was estimated as 6.65 $JK^{-1} mol^{-1}$. Another endothermic peak at −32.4 °C had a very small area due to the incomplete crystallization during the cooling process.

Physicochemical Properties of Pantolactone

Powder X-ray diffraction, IR and NMR measurements were made in order to characterize the transition at 62.0 °C of D-pantolactone. Figure 2 shows the IR spectra of D-pantolactone in the hydroxyl and carbonyl stretching regions. At 25 °C, intermolecular hydrogen-bonded hydroxyl and carbonyl stretchings were observed at about 3400 cm^{-1} and about 1770 cm^{-1}, respectively (Fig. 2A). Both bands were shifted to higher frequencies above 60 °C (Fig. 2C). In comparison with the CCl_4 solution spectrum of D-pantolactone,[5] the higher frequency shifts suggested that the intermolecular hydrogen bonds were weakened

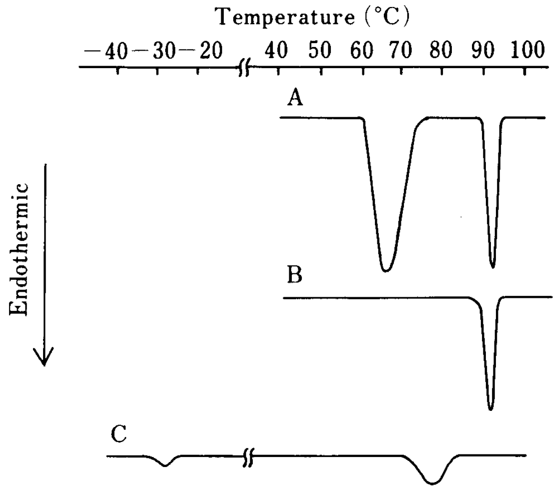

Fig. 1. DSC Curves of D- and DL-Pantolactone

A, D-pantolactone; B, rerun of sample A; C, DL-pantolactone.

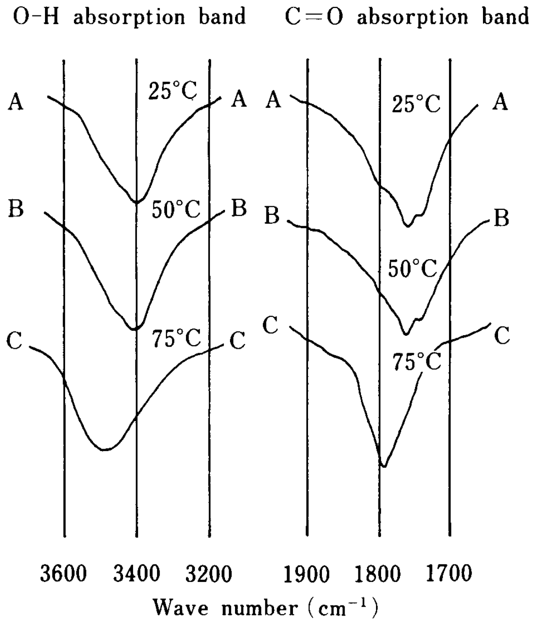

Fig. 2. IR Spectra of D-Pantolactone as a Function of Temperature

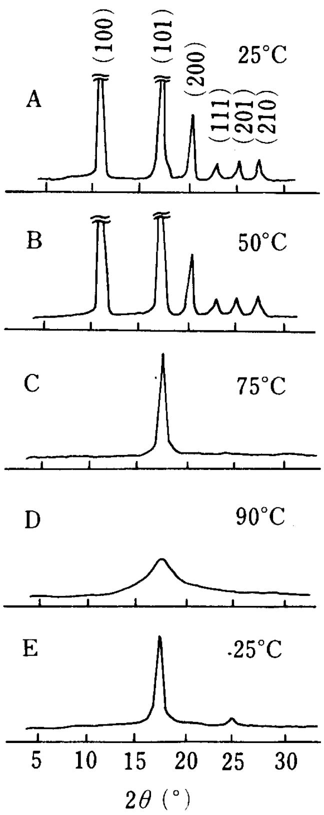

Fig. 3. Powder X-Ray Diffraction Patterns of D- (A—D) and DL- (E) Pantolactone as a Function of Temperature

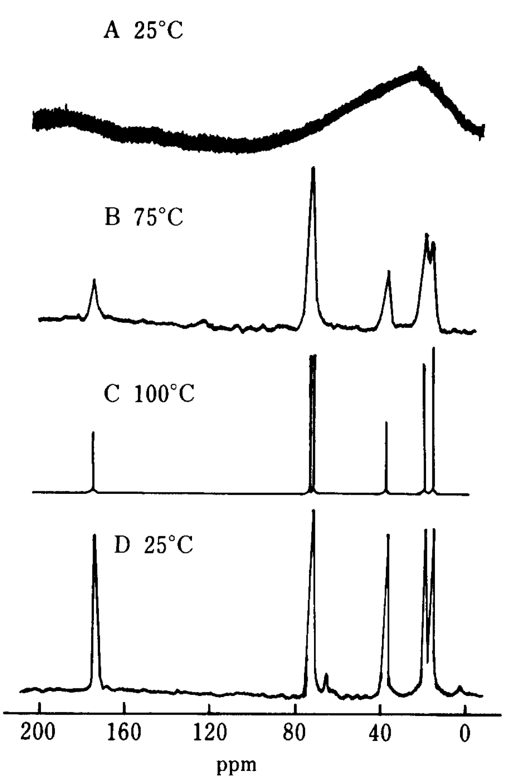

Fig. 4. ^{13}C Fourier Transform NMR Spectra of D- (A—C) and DL- (D) Pantolactone

The numbers of scans (N) were as follows: A, $N=500$; B, $N=500$; C, $N=150$; D, $N=100$.

after the first transition. Figure 3 shows the powder X-ray diffraction patterns of pantolactone crystals at various temperatures. The X-ray diffraction patterns of D-pantolactone differ significantly before and after the transition at 62 °C. The lattice constants of D-pantolactone at room temperature were calculated by the Hull–Davey method.[6] All diffraction lines could be very well assigned by assuming a hexagonal lattice with dimensions of $a=9.92$, $c=6.01$ Å. Most of the diffraction peaks of D-pantolactone disappeared after the transition at 62.0 °C and only one sharp peak at $2\theta=17.4°$ was observed at 75 °C (Fig. 3C). These phenomena leave the following possibilities: (1) a change of crystal form in the transition, (2) diffusion of diffraction peaks due to the decrease of structural order in the crystal, except for the peak at $2\theta=17.4°$. An X-ray crystal analysis which is in progress should clarify the reason for the powder diffraction pattern changes. Near the melting point, a broad peak around $2\theta=17.4°$ was observed (Fig. 3D). The peak intensity seemed a little stronger than that of the liquid. At room temperature, DL-pantolactone shows nearly the same diffraction pattern as D-pantolactone at 75 °C. Therefore, the molecular arrangement of DL-pantolactone at room temperature is probably the same as that of D-pantolactone between 62.0 and 91.6 °C. Figure 4 shows the ^{13}C-NMR spectra of D- and DL-pantolactone in the temperature range from room temperature to 100 °C (over the melting point). The NMR spectrum of D-pantolactone at room temperature was characterized by broad featureless curves because the solid sample showed ^{1}H–^{13}C dipolar broadening, long ^{13}C-spin lattice relaxation times and chemical shift anisotropy (Fig. 4A).[7] Above the melting point, every characteristic line was observed, because D-pantolactone was in the liquid state (Fig. 4C). It is remarkable that the spectral lines were resolved clearly at 75 °C, though the sample is apparently in the solid state (Fig.

4B). Yukitoshi *et al.* measured the NMR line width of plastic crystals of hexamethyldisilane and reported that the line width in the solid state was as narrow as in the liquid state.[8)] The narrowing of the absorption line width indicates rapid reorientational motion in the crystal lattice between 62.0 and 91.6 °C, suggesting the presence of a plastic crystal phase. For DL-pantolactone, the NMR spectral lines were clearly determined at room temperature (Fig. 4D). This also indicates that the reorientation of DL-pantolactone molecules was rapid at room temperature.

Walden's rule indicates that the entropy of melting for general organic crystals is about 56.5 $\mathrm{JK^{-1}\,mol^{-1}}$ (13.5 $\mathrm{calK^{-1}\,mol^{-1}}$) unless the molecules had any interaction in the liquid phase.[9)] Timmermans measured the thermodynamic values for many organic crystals.[10)] A plastic crystal, which was first proposed by Timmermans, had small ΔS_m (less than 20.9 $\mathrm{JK^{-1}\,mol^{-1}}$) while the sum of ΔS_t and ΔS_m is similar to the ΔS_m of general organic compounds (56.5 $\mathrm{JK^{-1}\,mol^{-1}}$).[10)] In the case of D-pantolactone, ΔS_m was 9.20 $\mathrm{JK^{-1}\,mol^{-1}}$, which is sufficiently less than 20.9 $\mathrm{JK^{-1}\,mol^{-1}}$. The sum of ΔS_t and ΔS_m was 53.6 $\mathrm{JK^{-1}\,mol^{-1}}$. This thermal behavior is consistent with the properties expected for a plastic crystal. DL-Pantolactone was also suggested to be in a plastic crystal state at room temperature, as ΔS_m was 6.65 $\mathrm{JK^{-1}\,mol^{-1}}$. ^{13}C-NMR spectroscopy also supported the existence of the plastic crystal state, because pantolactone behaves like a liquid at the mesophase, though the sample is apparently in the solid state.

From the results of thermal analysis, IR spectroscopy, powder X-ray diffraction, and ^{13}C-NMR spectroscopy, it was concluded that D-, L-, and DL-pantolactone exist as plastic crystals.

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