Optically Active and Racemic Glycerides. I. The Thermodynamic and Structural Relationship between Optically Active and the Corresponding Racemic α-Monostearins in Their Crystalline, Molten, and Dissolved States

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The thermodynamic and spectrographic properties, such as the melting temperature, the latent heat of fusion, the solubility, the heat of solution, and the infrared and NMR spectra, were studied for the stable β-forms of the optically active (*S*)- and the corresponding racemic (*RS*)-α-monostearin crystals. The phase diagram for the binary mixture and the IR spectra of (*S*)- and (*RS*)-crystals indicate that the (*RS*)- form is a racemic molecular compound consisting of (*R*)- and (*S*)-α-monostearin molecules. The latent heats of fusion for the (*S*)- and (*RS*)-α-monostearin crystals were 82.4 kJ mol^{-1} and 75.4 kJ mol^{-1} respectively. The heats of solution in benzene for the (*S*)- and the (*RS*)-crystals were 86.3 and 99.9 kJ mol^{-1} respectively. The difference in the heat of solution between the (*S*)- and the (*RS*)-crystals, $\Delta(\Delta H_S)$, was 13.6 kJ mol^{-1}, which may be attributable to the difference in the extent of hydrogen bonding. These results suggest that (*R*)- and (*S*)-molecules in the (*RS*)-form strongly interact to form a racemic pair not only in the crystalline state, but also in the molten state. Such a racemic pair dissociates into the free molecules when it is dissolved in a nonpolar solvent. The conclusion is supported by the IR and NMR spectra for both the glycerides in dissolved states.

The properties of α-monoglycerides, harmless detergents, have been studied by many investigators.[1–6] Little has yet been reported on the thermodynamic difference between optically active and (*RS*)-forms, however. The (*RS*)-form can, in general, be classified, in terms of the interaction of (*R*)- and (*S*)-molecules in the crystal, into three types of modification:[7,8] a racemic compound, a solid solution, or a mixture of (*R*)- and (*S*)-crystals. (*RS*)-α-Monoglycerides containing even carbon-chain lengths from C-12 to C-18 seem to be racemic compounds, as they appear at higher melting points than do their optically active (*S*)-forms.[9] The crystalline properties of the racemic compounds can be expected to differ from those of the optically active species. A comparative study has thus been made of the properties of these crystals: the thermodynamic and structural properties of the crystals of (*RS*)-α-monostearin were compared with those of (*S*)-α-monostearin in an effort to obtain knowledge of the interaction between (*R*)- and (*S*)-molecules in the racemic α-monostearin crystal.

Experimental

Materials. Pure (≫99%) samples of optically active (*S*)- and racemic (*RS*)-α-monostearins obtained from Fluka AG (Switzerland) were further purified by repeated recrystallizations from hexane. The melting points of these samples were 349.3 and 355.6 K respectively, in good agreement with the previously reported values[9] (349.2 K for (*S*)- and 355.2 K for (*RS*)-) for the β-form crystals. The polymorphic forms of the (*S*)- and (*RS*)-α-monostearins are the β, β′, α, and sub-α forms. The first one obtainable by slow crystallization from a solvent is the most stable[2,4,10] under ordinary conditions.

Apparatus and Procedures. The latent heat of fusion and the melting point were determined by the use of a differential scanning calorimeter (Shimadzu Model DSC-30) in the temperature range of 300—373 K at a constant rate of 5 K min^{-1} to rise the temperature. In order to obtain melting temperature-composition diagrams for mixtures of (*S*)- and (*RS*)-α-monostearins, they were mixed in benzene and allowed to stand overnight *in vacuo* to evaporate the solvent.** A standard sample of KNO_3[11] was used for calibration to obtain the latent heat of fusion. The solubility in benzene was determined at a constant temperature (±0.02 K) in the range of 281—298 K by the method of an asymptotic approach to the concentration-time curves for under- and super-saturated solutions.[12,13] About 10 h after the addition of a monostearin to the solvent, a 2.00 ml portion of a saturated solution was pipeted out through a glass tip covered with a piece of filter paper (Toyoroshi No. 5) which had been soaked in the solvent for 24 h prior to pipeting.[13] The pipeted solution was then evaporated to dryness *in vacuo* for weighing. The infrared spectra of the monostearins in crystalline state (in the KBr disks) and in the molten state (on the NaCl plate) were obtained with a Hitachi Model 260-10 spectrometer (resolving power of 0.5 cm^{-1}); those in CCl_4 solutions were obtained with a JASCO IR-A3 spectrometer (Japan Spectroscopic Co., Ltd.; resolving power of 0.7 cm^{-1}). The NMR spectra for those monostearins in benzene-d_6 (C_6D_6) were obtained with a JEOL-FX 60 NMR spectrometer.

Results and Discussion

The values of the melting point, the latent heat, ΔH_f, and the entropy, ΔS_f, of the fusion of (*S*)- and (*RS*)-α-monostearin crystals are listed on the second to fourth lines respectively in Table 1. The value of ΔH_f (75.4 kJ mol^{-1}) for the (*RS*)-form is in good agreement with that (75.4 kJ mol^{-1}) reported by T. Maruyama *et al.*[3]

Figure 1 shows the temperature dependences of the solubilities for the (*S*)- and (*RS*)-compounds in

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** Simple mixing of the two in a mortar always resulted in the appearance of two peaks on the DSC chart, the two giving a molar ratio exactly the same as that of the initial mixture. The peak positions also corresponded to the melting points for the mixture components.

benzene. The following van't Hoff equation was used to calculate the heat of solution, ΔH_s;

$$\ln C = \Delta H_s/RT + K, \quad (1)$$

where C is a solubility; R, the gas constant; T, the absolute temperature, and K, an integration constant. The activity coefficient was always assumed to be unity because of the low solubilities. The ΔH_s values are tabulated on the last line of Table 1.

In Fig. 2 the melting point is plotted against the mole fraction of (*RS*)-α-monostearin in the mixture of (*S*)- and (*RS*)-α-monostearins. The figure indicates that the (*RS*)-form is a typical racemic compound, giving an eutectic mixture at a molar ratio of 3:7. If there were a crystal of (*R*)-α-monostearin, it would have been of the same melting point as that for the crystal of the (*S*)-α-monostearin because enantiomers in general possess the same physical and chemical properties except in optical rotations and biological actions. The mp for the (*RS*)-form should thus give a maximum at an equilmolar mixture of the (*R*)- and (*S*)-compounds, implying that a racemic pair exists in the (*RS*)-crystal, as has been suggested by Larsson.[5,6] Such an implication leads to a more ordered arrangement of the molecules in the (*RS*)-crystal compared to the (*S*)-crystal, reflecting a kind of contradiction of the results on the third and fourth lines of Table 1: if we assume enthalpic and entropic identities between the liquid form (*S*)-crystal and (*RS*)-crystal, the former crystal should be in a more ordered state, with a lower enthalpy, than the latter. On the other hand, the ΔH_s values in Table 1 reveal a lower enthalpy for the (*RS*)-crystal, than that for the (*S*)-crystal, if we assume an identical state for a benzene solution of α-monostearin, whether it is (*S*) or (*RS*). In fact, the NMR pattern for a solution of the (*S*)-glyceride in benzene-d_6 (C_6D_6) was exactly the same as that of the (*RS*)-compound. The contradiction between the heat of fusion and that of solution can be clarified by assuming that the molten states of the (*S*)-form and the (*RS*)-form are different from each other. McGinn[14] has reported that "a liquid" of (*RS*)-octanol differs considerably from that of the (*R*)- or (*S*)-compound in its physical properties, such as density, boiling point, and refractive index.

The difference in the heat of solution between (*S*)- and (*RS*)-α-monostearin crystals, $\Delta(\Delta H_s)$, was 13.6 kJ mol^{-1}, which may be attributable to the difference mainly in the extent of hydrogen bonding. In fact, the OH-stretching vibration in the former crystal was different from that for the latter crystal, as shown in Fig. 3.

From the identity between (*S*)- and (*RS*)-compounds in the dissolved state and the assumption that their

Table 1. Thermodynamic properties of α-monostearins

	(*S*)-Form crystal	(*RS*)-Form crystal
Mp θ_m/K	349.3 349.2[10]	355.6 355.2[10]
Latent heat of fusion ΔH_f/kJ mol^{-1}	82.4	75.4 75.4[3]
Entropy of fusion ΔS_f/J K^{-1} mol^{-1}	235.9	212.0 213.4[3]
Heat of solution ΔH_s/kJ mol^{-1}	86.3	99.9

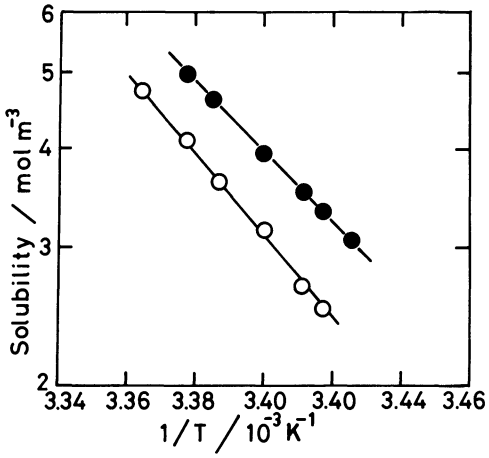

Fig. 1. Relationship between the solubilities and (1/*T*) for (*S*)- (filled symbols) and (*RS*)-α-monostearin (open) crystals.

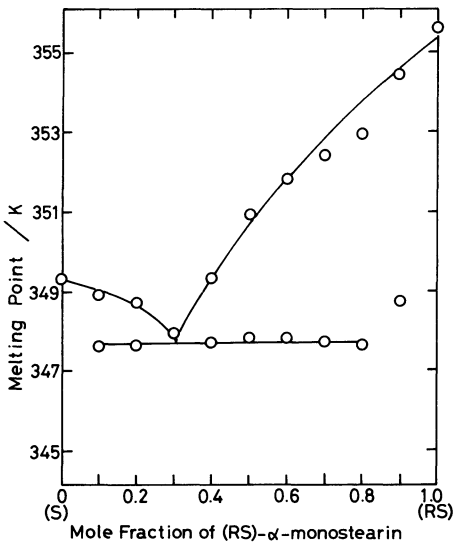

Fig. 2. Melting point of the mixture of (*S*)- and (*RS*)-α-monostearins as a function of the mole fraction of the (*RS*)-species.

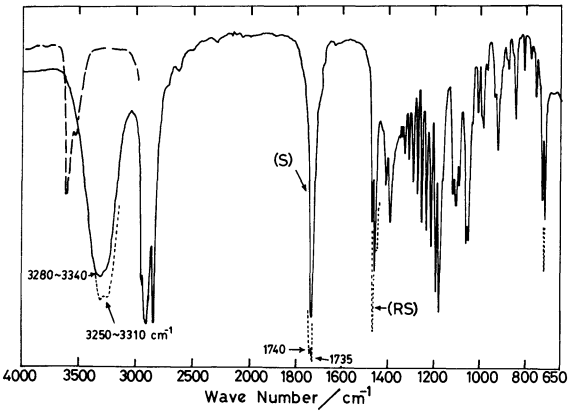

Fig. 3. Infrared spectra of α-monostearins:
Solid line expresses (*S*)-crystal in KBr disk, dotted one (*RS*)-, and dashed one (*S*)- or (*RS*)-forms in CCl_4.

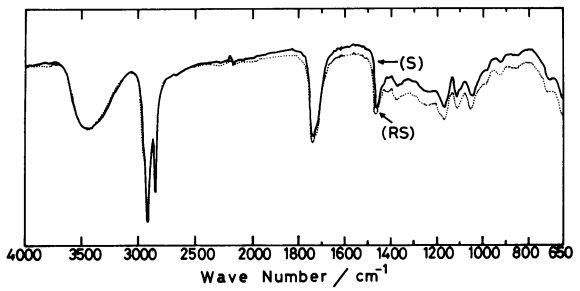

Fig. 4. Infrared spectra of α-monostearins in molten state at 358 K:
Solid line expresses (*S*)-form and dotted one (*RS*)-form on NaCl plate, respectively.

liquid states for (*S*)- and (*RS*)-crystals differ from each other, 20.6 [=(99.9 −75.4) −(86.3 −82.4)] kJ mol^{-1} can be calculated for the enthalpic difference between the molten (*S*)- and (*RS*)-forms, if we ignore the temperature difference between the solubility and the melting data. The enthalpic difference probably due to the difference in the intensities of the hydrogen bonding forces, the cohesive forces, and so on, between (*S*)- and (*S*)-molecules, and (*R*)- and (*S*)-molecules in their molten states. However, the IR spectra for their molten samples at 358 K did not show a remarkable difference between them, as shown in Fig. 4. The reason for that is uncertain at present.

Larsson[6] described that a unit cell of the (*S*)-α-monostearin contains eight molecules and is orthorhombic, with these dimensions; a=4.94 Å, b=8.97 Å, and c=100.4 Å, while in the (*RS*)-form, its unit cell contains also eight molecules, but gives monoclinic system with these dimensions; a=9.20 Å, b=100.5 Å, c=5.04 Å, and β=100.2°, giving a denser packing for the former as a whole. The racemic pair in the latter crystal should thus be arranged so as to give a lower density. Such a difference in the packing mode may contribute to the entropy difference $\Delta(\Delta S_f)$ between (*S*)-crystal → (*S*)-liquid (235.9 J K^{-1} mol^{-1}) and (*RS*)-crystal → (*RS*)-liquid (212.0 J K^{-1} mol^{-1}). Whatever the case, it must be stated that the $\Delta(\Delta H_f)$ difference is overwhelmed by the $\Delta(\Delta H_s)$ difference, so that the thermodynamic difference between (*S*)-crystal → (*S*)-liquid and (*RS*)-crystal → (*RS*)-liquid is much less than the thermodynamic difference between (*S*)-crystal → solution and (*RS*)-crystal → solution. This, in turn, implies that (*S*)-liquid is more different from (*RS*)-liquid than (*S*)-crystal is different from (*RS*)-crystal.

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