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ON THE DIMORPHISM OF DL-MALIC ACID

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ABSTRACT

The two crystalline forms of DL-malic acid have been studied by means of X-ray powder diffraction and differential thermal analysis. The stable form I melts at 402 K ($\Delta_{fus}H_I = 250$ J g^{-1}). The metastable form II melts at 396 K ($\Delta_{fus}H_{II} = 225$ J g^{-1}). It can be concluded from structural and thermodynamic data that form I is the stable form and form II is probably a high-pressure modification. Furthermore, the high values of the entropies of fusion of both forms show that, in these phases, the molecules do not undergo large-amplitude motion.

INTRODUCTION

The phase diagram of the malic acid enantiomers is described as having an inflexion point in the liquidus curve at $x = 0.25$ [1], the existence of which has been connected to an ‘anomalous racemate’ formed by the enantiomers in the ratio 1 : 3. This compound has been identified by X-ray powder diffraction.

Others authors [2] have found that DL-malic acid undergoes a polymorphic phase transition. These authors explain the inflexion point by assuming that the stable (I) and the metastable (II) forms are in equilibrium with L-malic acid in the composition ranges $0.25 < x < 0.5$ and $0 < x < 0.25$, respectively. The crystal structures of form I [3] and form II [4] have been determined. Both forms consist of linear chains of malic acid molecules.

The present work has been undertaken in order to obtain quantitative data on the melting of both forms, and information on the lifetime of form

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II, by means of differential thermal analysis (DTA) and X-ray powder diffraction measurements.

EXPERIMENTAL

DTA results were obtained by means of a Mettler FP 800 analyser connected to an Epson HX20 computer. The samples were weighed using a microbalance sensitive to 0.01 mg. X-ray diffraction data were obtained using an Enraf-Nonius FR552 camera.

Commercial DL-malic acid corresponds to stable form I, as shown by its X-ray diffraction spectrum. Metastable form II was obtained by evaporating a solution of form I in acetone.

RESULTS

X-ray diffraction studies

Although the lattices of both forms are very similar (see Table 1), the respective X-ray spectra can easily be distinguished (see Fig. 1).

The interplanar distances have been calculated, and the values (d_{calc}) are in good agreement with d_{obs} values in both cases (Tables 2 and 3) and with the data previously given for form I [1].

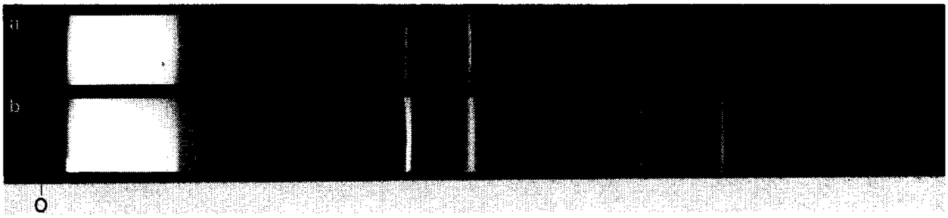

Fig. 1. X-ray diffraction spectra obtained using λ Cu $K\alpha_1 = 1.5405$ Å, 50 kV, 20 mA, 1 h. A, DL-malic acid, form I; B, DL-malic acid, form II; o, trace of the incident X-ray beam.

TABLE 1

Crystal data for forms I and II of DL-malic acid ($C_4H_6O_5$, MW = 134.09) from refs. 3 and 4, respectively

Form	Crystal structure	Space group	Cell parameters						Z	V (Å^3)
			a (Å)	b (Å)	c (Å)	α (deg)	β (deg)	γ (deg)		
I	Monoclinic	$P2_1/c$	4.889	8.815	13.036	90.0	102.93	90.0	4	547.6
II	Monoclinic	Cc	13.053	8.724	4.878	90.0	103.31	90.0	4	540.6

TABLE 2

X-ray powder diffraction data (this work, unless otherwise indicated) for form I of DL-malic acid

d_{obs} (Å)	I [a]	d_{obs} (Å) from ref. 1	I from ref. 1	d_{calc} (Å)	$h\,k\,l$
7.27	vw	–	–	7.243	0 1 1
6.38	w	–	–	6.353	0 0 2
4.77	w	4.79	w	4.765	1 0 0
4.41	s	4.405	s	4.408	0 2 0
4.31	w	–	–	4.302	$\bar{1}$ 0 2
4.237	m	4.238	w	4.237	$\bar{1}$ 1 1
3.764	vs	3.761	s	3.766	1 1 1
3.627	vw	3.654	w?	3.621	0 2 2
3.460	vw?	–	–	3.459	1 0 2
3.332	mw	3.335	w	3.324	$\bar{1}$ 1 3
3.259	w	–	–	3.236	$\bar{1}$ 2 1
3.219	m	3.227	m	3.219	1 1 2
3.174	mw	–	–	3.176	0 0 4
3.088	vw?	–	–	3.078	$\bar{1}$ 2 2
3.056	vw	–	–	3.054	0 2 3
2.819	vw	–	–	2.812	$\bar{1}$ 1 4
2.784	vw	–	–	2.783	$\bar{1}$ 2 3
2.734	m	–	–	2.723	1 1 3
2.726	ms	2.727	m	2.721	1 2 2
2.667	vw	–	–	2.667	0 3 2
2.503	w	2.513	w	2.510	$\bar{1}$ 3 1
				2.501	1 3 0
2.421	w	2.416	w?	2.426	1 0 4
				2.406	1 0 4
2.392	s	2.393	m	2.401	1 2 3, 1 3 1
2.386	m	–	–	2.392	$\bar{1}$ 1 5
				2.382	2 0 0
2.353	vw?	–	–	2.354	$\bar{2}$ 1 1
2.317	vw?	–	–	2.300	2 1 0
2.272	vw	–	–	2.274	$\bar{1}$ 3 3
2.237	m	2.240	w	2.239	1 3 2
2.203	w	2.200	w	2.204	0 4 0
				2.201	0 2 5
2.152	w	2.153	w	2.157	0 3 4
				2.151	$\bar{2}$ 0 4
2.110	w	–	–	2.119	$\bar{1}$ 0 6
				2.118	$\bar{2}$ 2 2, 0 0 6
				2.112	1 2 4
2.096	vw	–	–	2.096	2 2 0
2.080	vw	2.082	w	2.083	2 0 2
				2.082	0 4 2
2.044	m	2.045	w	2.051	1 3 3
				2.045	$\bar{2}$ 2 3
2.003	vw	2.008	w	2.005	2 2 1, 1 1 5, 1 4 1

[a] v, Very; m, medium; w, weak; s, strong; ?, dubious.

TABLE 3

X-ray powder diffraction data for form II of DL-malic acid

d_{obs} (Å)	I [a]	d_{calc} (Å)	$h\,k\,l$
6.36	w	6.35	2 0 0
4.38	vs(b)	4.362	0 2 0
3.75	s(b)	3.809	3 1 0
		3.744	1 1 1
3.62	vw?	3.596	2 2 0
3.336	m(b)	3.326	$\bar{3}$ 1 1
3.189	m(b)	3.176	4 0 0
2.718	s(b)	2.710	3 1 1
2.704	s(b)	2.702	2 2 1
2.576	vw	2.567	4 2 0
2.500	vw(b)	2.491	$\bar{1}$ 3 1
2.466	vw	2.458	$\bar{4}$ 2 1
2.418	vw	2.413	$\bar{2}$ 0 2
2.402	s	2.397	3 3 0
		2.395	$\bar{5}$ 1 1
		2.381	1 3 1
2.236	vw?	2.233	$\bar{3}$ 1 2
2.189	vw	2.181	0 4 0
2.162	mw	2.171	1 1 2
		2.154	$\bar{4}$ 2 0
2.120	vw	2.117	6 0 0
		2.100	4 2 1
2.067	vw?	2.085	0 2 2
		2.063	2 4 0
2.002?	vw	1.997	5 1 1
		1.982	0 4 1

[a] v, Very; m, medium; w, weak; s, strong; ?, dubious; (b), broad.

Thermal studies

Preliminary results had shown that the fusion temperatures $(T_{fus})_I$ and $(T_{fus})_{II}$ and the enthalpies of fusion $\Delta_{fus}H_I$ and $\Delta_{fus}H_{II}$ are only slightly different for the two forms, and that melting of form II is not followed by recrystallization of form I. Enthalpies of fusion of form II samples were therefore measured as a function of time and compared with that of a commercial form I sample (Chemical Company GmbH, F.R.G.). Results obtained over a 140 day period are given in Fig. 2.

Using heating rates of 3 K min^{-1} and 5 K min^{-1}, form I melts at 402 K ($\Delta_{fus}H_I = 250$ J g^{-1}) and form II at 396 K ($\Delta_{fus}H_{II} = 225$ J g^{-1}). These temperature values agree with results from ref. 2 for both forms and with those from ref. 5 for form I.

It should be noted that ground samples undergo the II → I transformation within only a few (ca. 5) days, whereas unground samples (chosen in two

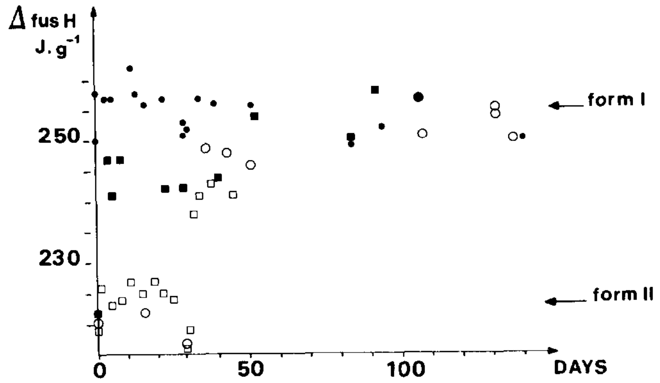

Fig. 2. Enthalpies of fusion as a function of time for commercial samples of form I (●) and form II (■, ground batch; ○ and □, unground batches). All batches were stored at room temperature (288–293 K).

different batches) do not transform for a month or so. After this time, $\Delta_{\text{fus}}H_{\text{I}}$ is determined. These observations agree with those of X-ray determinations.

According to Gabard and Collet [6], the Gibbs free energies $\Delta G^{\text{f}}(T)$ for the formation reactions, D(cryst.) + L(cryst.) → DL(cryst.), have been calculated at 373 K, close to the lowest T_{fus} value. Therefore, T_{fus} and $\Delta_{\text{fus}}H$ for D- or L-malic acid had to be measured. Using Schuchardt D- and Merck L-malic acid samples (5 measurements on each), values obtained were $(T_{\text{fus}})_{\text{A}} = 376$ K (A ≡ optically active) and $\Delta_{\text{fus}}H_{\text{A}} = 200$ J g^{-1}.

According to the relationship given in ref. 6

$$\Delta G^{\text{f}}(T) = [\Delta_{\text{fus}}H_{\text{A}} - \Delta_{\text{fus}}H_{\text{DL}} - T(\Delta_{\text{fus}}S_{\text{A}} - \Delta_{\text{fus}}S_{\text{DL}})] - RT \ln 2 + f(C_p, T) \tag{1}$$

in which the term in square brackets is the intrinsic stability difference ΔG^{i}. Neglecting $f(C_p, T)$, we obtained $\Delta G^{\text{f}}_{\text{I}} = -5.85$ kJ mol^{-1}, $\Delta G^{\text{i}}_{\text{I}} = -3.55$ kJ mol^{-1}, $\Delta G^{\text{f}}_{\text{II}} = -4.0$ kJ mol^{-1} and $\Delta G^{\text{i}}_{\text{II}} = -1.81$ kJ mol^{-1}.

DISCUSSION AND CONCLUSION

The measured X-ray diffraction lines of five different batches of form II are always significantly broader than those of form I. It can be inferred that form II is disordered at room temperature.

From structural results (X-ray and IR), it was assumed by van Loock et al. [4] that "the low stability of form II may be caused by the absence of hydrogen bridges between the chains, thus opening the possibility of free rotation around the –CH–OH group". This hypothesis agrees with the decomposition of single crystals, which are transformed into white powders within a few minutes [4], one week [2] or one month (this work).

It may also be considered, using data from ref. 4, that form II malic acid molecules are enclosed in head-to-tail aligned up cylinders of ca. 2.4 Å radius that can freely rotate together around their axes without change of the unit-cell volume (the mirror planes have to be preserved), since the shortest distance between two neighbouring chains is ca. 3.08 Å.

However, the entropy of fusion of form II (75 J K^{-1} mol^{-1}) is not significantly different from that of form I (79 J K^{-1} mol^{-1}), in which the malic acid chains are hydrogen bonded [3]. Furthermore, these fusion entropies are much larger than the value of 21 J K^{-1} mol^{-1} which, according to Timmermans [7], indicates that a crystalline phase is plastic.

This means that the disorder in form II is probably static.

Our calorimetric results agree with the observed spontaneous II → I transformation and with the ΔG^{f} and ΔG^{i} values obtained by Gabard and Collet [6] with some 2-phenoxypropionic acids, although our $\Delta_{\mathrm{fus}}H$ values for malic acids differ from those given by Jacques et al. [5].

It may be noted that form II is non-centrosymmetric and is less stable than form I, although the molecular volume, V, of II is lower than that of I. This disagrees with the usual rule, according to which the stabler phase is the denser one, although the stability order agrees with the fact that form I contains more hydrogen bonds than does form II. It can therefore be predicted that phase II will be stable under high pressures.

In the case of the DL-malic acid II → I transition, using the relationship

$$\Delta H_{\mathrm{II}\rightarrow\mathrm{I}} = \Delta_{\mathrm{fus}}H_{\mathrm{I}} - \Delta_{\mathrm{fus}}H_{\mathrm{II}} = 3.3\ \mathrm{kJ\ mol}^{-1} \qquad (2)$$

with $T_{\mathrm{fus}} = 400$ K and $V_{\mathrm{II}} - V_{\mathrm{I}} = -1.75$ Å^3 per molecule [3,4], and assuming that ΔV remains almost constant when P and T change, it is found that $\mathrm{d}P/\mathrm{d}T$ is ca. -5.3 MPa K^{-1}.

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