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Polymorphism and thermal behaviour of 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acid

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Abstract

The polymorphism of 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acid was investigated by differential scanning calorimetry, X-ray diffractometry and infrared spectroscopy. Three types of intermolecular hydrogen bonds can occur. In the first two, cyclic dimers are formed by intermolecular associations between carboxylic groups whose C–O bond lengths either differ or are almost equal, while the ketone carbonyls remain uninvolved. The third type is an intermolecular carboxyl-to-ketone hydrogen bond repeated infinitely to yield a chain.

INTRODUCTION

We have previously analysed *ortho*-aryl and allo-aryl camphoric acid derivatives by infrared spectroscopy and have characterized their thermal behaviour [1]. A thermoanalytical study of an entire homogeneous series of cis form (α) 3-aryl-1,2,2-trimethyl cyclopentane carboxylic acids was also recently carried out by our laboratory [2].

These studies allowed us to determine the structural criteria required to recognize possible tautomeric hydroxy-lactones (γ) formed for such γ-carbonyl acids and demonstrated the diversity of the thermal behaviour of this type of compound.

Tautomeric amorphous or glassy compounds have been obtained by rapid cooling of melted samples, which also led to polymorphism. The

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structures of two forms of 3-*para*-thioanisoyl-1,2,2-trimethyl cyclopentane carboxylic acid (1R, 3S) were investigated [3, 4].

We report our results on racemic and laevo-rotatory 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acids (where R is $-CH_3$) which complement our previous studies on this optically active compound, which revealed four polymorphic modifications [5].

EXPERIMENTAL

Apparatus

The differential scanning calorimetry was performed with a Perkin-Elmer DSC-4 connected to a 3600 computer, with indium used as the thermometric and calorimetric standard.

All calorimetry was carried out under flowing nitrogen, with 2–3 mg samples in sealed capsules, heated at 20°C min^{-1}. After melting, all samples were cooled rapidly at 320°C min^{-1} and then reheated at 20°C min^{-1}.

Transparency modifications in the samples, due to phase changes during melting or crystallization, were measured with a Mettler automatic melting analyser fitted with an FP1 oven and FP1 programmer.

X-ray diffractograms were obtained on a CGR goniometer with a monochromator and a copper anti-cathode ($K\alpha = 1.5405$ Å), scanned at a rate of $15°\theta\,h^{-1}$, the adjustment was checked with diffractograms of a gypsum control sample. The reproducibility of the measurements was 2/100 of a degree for the entire X-ray measurement.

Infrared spectra were measured with a Perkin-Elmer spectrophotometer model 983 G, in the 4000–200 cm^{-1} region. For comparison, samples were suspended in Nujol and compressed in potassium bromide pellets.

The rotatory power was measured in chloroform with a Carl-Zeiss apparatus.

A Leitz heating-stage polarizing microscope was used for the thermomicroscopic analysis.

Reagents

Racemic (**1**) and laevo-rotatory (**2**) 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acids were prepared by reacting camphoric anhydride (racemic or optically active) with toluene in the presence of aluminium chloride [6]. The racemic compound **1** was crystallized in a benzene–petroleum ether mixture and had a melting point of 178°C. (The instant melting points were all measured on a Kofler scale without correction.)

The levo-rotatory acid **2** was crystallized in a methanol-water mixture (**2.1**) or in toluene (**2.2**). Each crystallized product was divided into two parts, and pressure dried and reduced at 80°C (**2.1.1**; **2.2.1**) and at 110°C (**2.1.2**; **2.2.2**), respectively.

All samples obtained from acid **2** had the same rotatory power $[\alpha]_{D20} = -76.6°$. They all melted at 195°C, except for samples **2.2.1** and **2.1.2** which had melting points of 193 and 189°C, respectively.

RESULTS

Infrared spectroscopy

The infrared spectra of all the compounds studied showed a characteristically tautomeric (α) form. They were analysed and the vibrational modes were assigned as $\delta_{AC}(OH)$, $\gamma_{AC}(OH)$, $\nu_{AC}(C{=}O)$ and $\nu_{AC}(C{-}O)$ of the carboxylic group and $\nu_{CE}(C{=}O)$ of the ketone carbonyl (Table 1).

It should be noted that samples **2.1**, **2.2**, **2.1.1**, **2.2.1** and **2.2.2** showed

TABLE 1

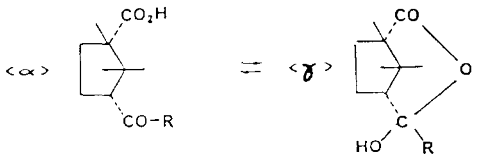
Infrared frequencies (cm^{-1}) for carboxylic and ketonic groups of 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acids

	$\delta_{AC}(OH) +$ $\nu_{AC}(C{-}O)$	I	$\nu_{AC}(C{-}O) +$ $\delta_{AC}(OH)$	I	$\nu_{AC}(C{=}O)$	I	$\nu_{CE}(C{=}O)$	I	$\gamma_{AC}(OH)$	I
1	1409	M	1288	M	1693	F	1662	F	942	M
2.1										
VI[a]	1407	M	1273	F	1687	F	1667	F	953	M
II[b]	1408	M	1288	f	1691	F	1665	F	951	f
2.2										
VII[a]	1407	M	1275	M	1687	F	1666	F	953	M
II[b]	1408	M	1288	M	1690	F	1664	F	951	f
2.1.1										
IV[a]	1407	M	1274	M	1687	F	1666	F	954	M
II[b]	1408	M	1288	M	1688	F	1664	F	948	M
2.2.1										
V[a]	1407	M	1274	M	1687	F	1666	F	956	M
III[b]	1408	M	1288	M	1694	F	1664	F	938	M
2.1.2										
I[a]	1409	M	1289	M	1694	F	1664	F	938	M
2.2.2										
II[a]	1408	M	1289	M	1690	F	1665	F	950	M

[a] Original samples.

[b] Samples heated to above the previous endothermic melting temperature.

Key: M, medium; F, strong; f, weak.



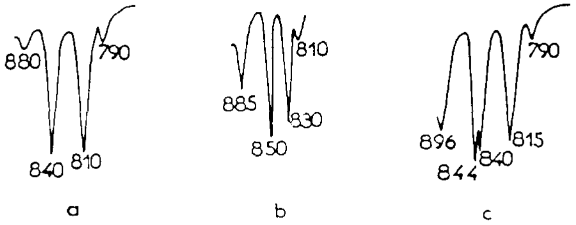


Fig. 1. Infrared spectra in the 900–760 cm^{-1} range: (a) compounds **2.1**, **2.2**, **2.1.1**, **2.2.1**, **2.2.2**; (b) compound **2.1.2**; (c) compound **1**.

identical spectra in the 895–795 cm^{-1} range (Fig. 1(a)), whereas spectra for samples **2.1.2** (Fig. 1(b)) and **1** (Fig. 1(c)) are different. In the study of carboxylic group modes, only compound **2.1.2** showed a different spectrum; in particular, the γ_{AC}(OH) bending vibration shifted towards lower frequencies at 938 cm^{-1}.

Differential scanning calorimetry

Compound 1

The racemic compound **1** melted at 173.2°C, with a melting enthalpy of 124 ± 0.5 J g^{-1} (Fig. 2(a)). After rapid cooling, light transmission through the sample was about 70%. During reheating, after a slight variation in the thermogram baseline which indicated glass transition at 32°C ($\Delta C_p = 0.5$ J g^{-1} K^{-1}), the sample suddenly lost its transparency as it completely crystallized at 72°C ($\Delta H_c = -16.1$ J g^{-1}). This transparency again peaked when the sample melted in two stages at 168 and 173°C (Fig. 2(b)).

However, the light transmission through the cooled sample increased progressively during the following two heating–cooling cycles. This was also the case for the intensity of the exothermic crystallization, with a maximum enthalpy of crystallization of −47 J g^{-1} (Fig. 2(b), 2(c), 2(d)). Moreover, the intensity of the new endotherm at 168°C increased progressively until it represented the entire melting phenomenon ($\Delta H_F = 104.5 \pm 0.5$ J g^{-1}) (Fig. 2(c), 2(d)).

This phenomenon, noted in the differential scanning calorimetry, was manifested as modifications in the X-ray diffractograms (Fig. 3), whereas

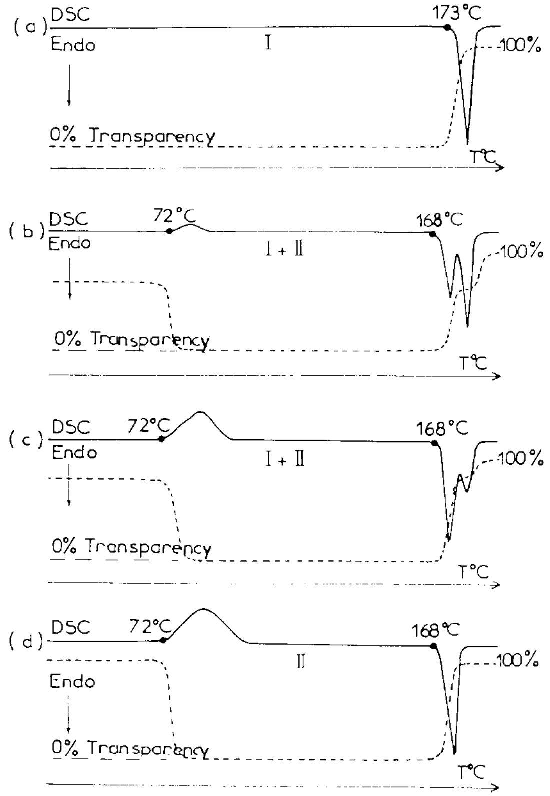


Fig. 2. DSC and transparency curves obtained for compound **1** during the first temperature increase and: (a) further temperature increases; (b) the first thermal treatment; (c) the second thermal treatment; (d) the third thermal treatment.

infrared spectra for the initial product **1** and the rapidly cooled samples were identical. This indicated the formation of a new crystalline product with a melting point of 168°C. Rapid and repeated cooling of the melted initial high form favoured the formation of this new product ($T_F = 173°C$).

This type of behaviour was previously described for other compounds in the same series [1, 2]. These forms are clearly obtained by dimer formation via the standard associations between carboxylic groups with almost identical [3] or different [4] CO bond lengths.

Compound 2

Analysis of the thermograms (Fig. 4) revealed only one endothermic failure in the two samples dried under reduced pressure at 110°C. This endotherm appeared at 195°C (Fig. 4(c)) for compound **2.1.2**, crystallized in a methanol–water mixture, and at 191°C (Fig. 4(f)) for compound **2.2.2**, crystallized in toluene. The other samples melted at 191°C, (**2.1**, **2.1.1**, **2.2**) and at 188.8°C (**2.2.1**) and showed a second endothermic failure.

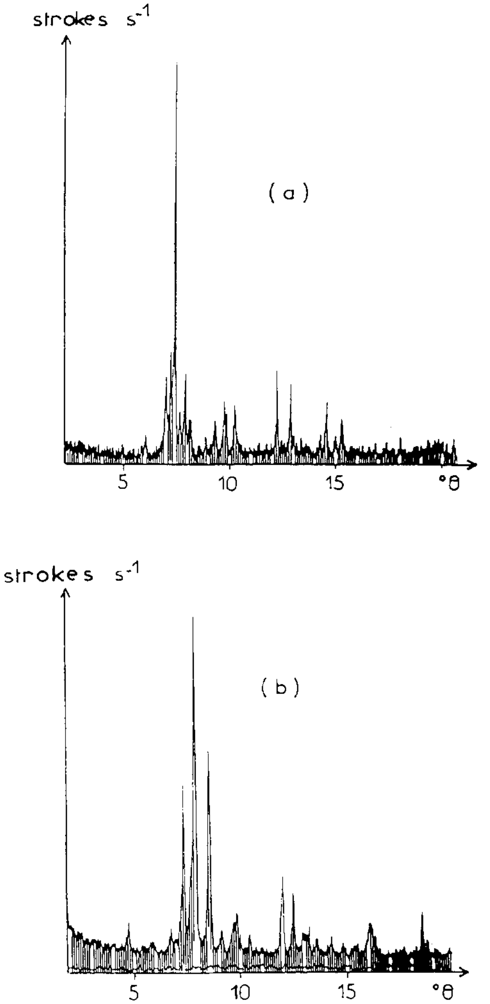


Fig. 3. X-ray diffractograms for compound **1**: (a) form **I** ($T = 173°C$); (b) form **II** ($T = 168°C$).

This second endotherm occurred at 114°C (**2.1.1**; Fig. 4(b)) and at 110°C (**2.2.1**; Fig. 4(e)) in samples dried at 80°C. It appeared at 106°C (**2.1**; Fig. 4(a)) and at 98°C (**2.2**; Fig. 4(d)) for samples obtained at room temperature. Except for compound **2.2.1**, there were no transparency changes for this endotherm, thus indicating a solid–solid transition.

In contrast, compound **2.2.1** showed partial melting of diamond-shaped crystals at 110°C ($\Delta H = 19.2\ \mathrm{J\ g^{-1}}$), immediately followed by low-energy formation of needle-shaped crystals ($\Delta H = -5.2\ \mathrm{J\ g^{-1}}$). This frequently noted phenomenon is termed heterogeneous melting [7].

All samples with two endotherms were assessed by infrared spectroscopy and X-ray diffractometry before and after the second endotherm.

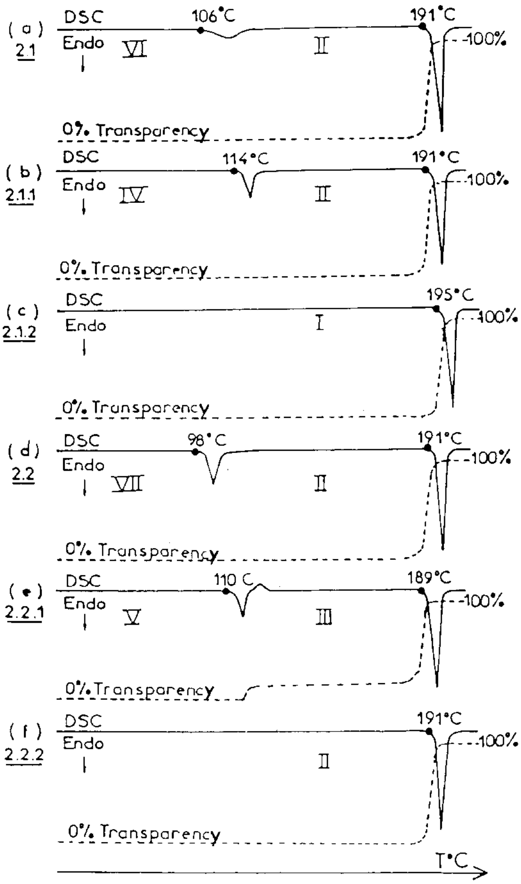


Fig. 4. DSC and transparency curves for compounds: (a) **2.1**; (b) **2.1.1**; (c) **2.1.2**; (d) **2.2**; (e) **2.2.1**; and (f) **2.2.2**.

According to these analyses, samples **2.1**, **2.2** and **2.1.1** had infrared spectra and X-ray diffractograms identical to those of **2.2.2** when heated to above the transition temperature. However, the spectra for samples **2.1.2** and **2.2.1** heated to 130°C were quite similar, whereas their X-ray diffractograms differed substantially (Table 1).

From these results, crystalline modifications at melting points of 195°C (**2.1.2**), 191°C (**2.2.2**) and 188.8°C were designated as **I**[5], **II**[5] and **III**, respectively; samples **2.1.1**, **2.2.1**, **2.1** and **2.2** were classified in decreasing order of their transition temperatures as **IV**, **V**, **VI** and **VII** respectively.

The mean melting point and transformation temperatures, with corresponding enthalpies, are given in Table 2.

X-ray diffractometry

Characteristic X-ray patterns of all the polymorphs are given in Tables 3 and 4. The highest intensity patterns were noted at 7.83°θ for **I**, 7.80°θ for **II**

TABLE 2

Summary of the melting and transition temperatures and enthalpies of various crystalline modifications in laevo-rotatory 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acid **2**

Transiton	Temperature/°C	Enthalpy/(J g^{-1})
I (2.1.2) → Liquid	195.0 ± 0.5	110.0 ± 0.7
II (2.1.2) → Liquid	191.1 ± 0.5	106.6 ± 0.5
III → Liquid	188.8 ± 0.5	98.9 ± 0.4
IV (2.1.1) → **II**	114.0 ± 0.7	23.1 ± 0.7
V (2.2.1) → **III**	109.6 ± 0.5	19.2 ± 0.6
VI (2.1) → **II**	106.1 ± 0.5	15.0 ± 0.3
VII (2.2) → **II**	98.0 ± 0.3	14.1 ± 0.5

and 7.82°θ for **III**. Highest intensity patterns in forms **V** and **VII** were observed at 6.86°θ and 6.87°θ respectively, and at 7.37°θ for **IV** and 14.20°θ for **VI**.

Diffraction peaks obtained for form **I** were completely different from those of forms **IV** and **VI**. In contrast, the peak at 12°θ was also noted in forms **II** and **III**, at 7.30°θ in forms **V** and **VII**, at 7.83°θ in form **V**, and at 9.60°θ and 12.50°θ in forms **III** and **V**.

The diffraction peaks for form **II** were completely different from those of form **V**, but peaks at 4.24°θ, 5.99°θ, 6.90°θ, 11.24°θ and 12.80°θ were also noted in form **VI**, and at 7.39°θ and 8.60°θ in form **VII**.

Concerning form **III**, the peak at 10.40°θ was also noted in forms **IV** and **VII**, at 10.60°θ in form **VII**, and also the peak at 14.20°θ was the most intense peak in form **VI**.

DISCUSSION

Considering the melting heat laws [8, 9], we conclude that forms **I** and **II**, **I** and **III**, and **II** and **III** are monotropic. Of any of these pairs of forms, the one that melted at the highest temperature also had the highest melting heat (Fig. 5). Therefore, the two free enthalpic isobars could only meet when the two forms were in the liquid state.

In contrast, the transition heat law [8, 9] states that endothermic transformation only involves enantiotropic forms, which is the case for **IV** and **II**, **VI** and **II**, and **VII** and **II**.

Thermal treatment did not modify the fusion temperature of the crystalline forms, except for form **I** which melted at 191°C during reheating. Moreover, thermal treatment revealed two different behavioural patterns.

TABLE 3

Diffraction angles, crosslinking distances and intensity ratios of forms **I**, **II** and **III** in laevo-rotatory 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acid **2**

I (2.1.2)			**II (2.2.2)**			**III (2.2.1)**		
Degrees θ	$d_{(\mathrm{obs})}$/Å	I/I_0	Degrees θ	$d_{(\mathrm{obs})}$/Å	I/I_0	Degrees θ	$d_{(\mathrm{obs})}$/Å	I/I_0
4.75	9.301	12	4.24	10.418	6	2.85	15.491	11
5.85	7.557	8	4.80	9.205	8	3.63	12.165	10
6.73	6.572	8	5.99	7.381	18	4.78	9.243	10
7.30	6.061	40	6.80	6.505	25	4.84	9.129	13
7.83	5.653	100	6.90	6.411	37	5.90	7.493	4
8.54	5.186	50	7.33	6.037	59	6.50	6.804	10
9.14	4.849	9	7.39	5.988	55	7.34	6.029	37
9.60	4.618	18	7.80	5.675	100	7.82	5.661	100
10.35	4.287	12	7.89	5.611	87	8.59	5.156	52
10.98	4.040	8	8.24	5.374	13	9.15	4.843	6
12.00	3.704	37	8.50	5.214	31	9.60	4.618	15
12.50	3.558	25	8.60	5.150	32	10.40	4.266	7
13.00	3.424	11	9.67	4.585	23	10.95	4.054	7
14.00	3.183	11	10.09	4.396	14	11.39	3.900	20
16.00	2.794	12	10.39	4.270	21	12.00	3.704	41
18.72	2.399	8	11.24	3.951	13	12.50	3.558	27
			11.43	3.886	22	13.10	3.421	8
			11.93	3.726	15	14.20	3.139	16
			12.00	3.704	69	14.82	3.011	14
			12.53	3.550	31	16.10	2.777	10
			12.80	3.476	38	18.55	2.421	5
			13.17	3.380	12	18.74	2.396	5
			14.17	3.146	18			
			14.26	3.127	18			
			14.39	3.099	32			
			15.77	2.834	11			
			16.17	2.765	13			
			16.44	2.721	10			
			18.33	2.449	10			
			18.80	2.390	8			
			18.94	2.373	8			

The first concerned form **V** which became amorphous when melted and cooled rapidly. It then crystallized at 60.5°C during reheating, with endothermic transition occurring at 123°C.

Thermomicroscopic analysis of this phenomenon revealed that rapid cooling of a melted form **V** sample resulted in a combination of forms **III** and **V**, which are readily differentiated morphologically. When heated, there was a greater abundance of needle-shaped crystals (**III**) which melted at 188°C, whereas diamond-shaped crystals (**V**) appeared at 123°C.

TABLE 4

Diffraction angles, crosslinking distances and intensity ratios of forms **IV**, **V**, **VI** and **VII** in laevo-rotatory 3-*para*-toluyl-1,2,2-trimethyl cyclopentane carboxylic acid **2**

IV (2.1.1)			**V (2.2.1)**			**VI (2.1)**			**VII (2.2)**		
Degrees θ	$d_{(obs)}$/Å	I/I_0	Degrees θ	$d_{(obs)}$/Å	I/I_0	Degrees θ	$d_{(obs)}$/Å	I/I_0	Degrees θ	$d_{(obs)}$/Å	I/I_0
5.97	7.405	39	4.16	10.618	10	4.34	10.442	10	4.22	0.467	9
6.85	6.458	5	5.96	7.418	45	5.99	7.381	66	5.98	7.393	34
7.37	6.004	100	6.86	6.448	100	6.90	6.411	56	6.87	6.439	100
7.85	5.639	31	7.30	6.061	75	7.36	6.012	36	7.30	6.061	70
8.23	5.380	22	7.34	6.029	68	7.40	5.980	32	7.39	5.988	52
8.43	5.254	29	7.83	5.653	26	7.87	5.625	11	7.88	5.618	42
9.30	4.776	13	8.20	5.400	26	8.16	5.426	9	8.25	5.367	18
9.85	4.502	64	8.46	5.235	56	8.26	5.361	10	8.48	5.223	50
10.09	4.396	48	9.26	4.785	11	8.47	5.229	38	8.60	5.150	11
10.40	4.266	26	9.60	4.618	9	9.34	4.746	7	9.10	4.870	11
11.23	3.955	20	9.80	4.525	12	9.86	4.498	81	9.65	4.594	11
11.46	3.876	23	10.05	4.413	34	10.10	4.392	26	9.86	4.498	11
12.05	3.689	29	10.36	4.283	25	10.40	4.266	18	10.07	4.405	24
12.36	3.598	12	10.60	4.187	15	10.60	4.187	13	10.40	4.266	21

12.53	3.550	16	11.20	3.965	25	11.24	3.951	13	10.65	4,167	17
12.78	3.482	40	11.46	3.876	55	11.50	3.860	29	11.23	3.955	18
14.18	3.144	43	12.02	3.698	32	12.10	3.674	62	11.47	3.873	56
14.35	3.107	44	12.50	3.558	20	12.37	3.595	9	12.05	3.689	32
14.85	3.005	17	12.73	3.495	76	12.44	3.575	10	12.55	3.544	21
15.77	2.834	8	14.13	3.155	52	12.80	3.476	86	12.75	3.490	70
16.43	2.723	30	14.36	3.105	82	14.20	3.139	100	14.06	3.170	39
16.90	2.649	10	15.74	2.839	23	14.40	3.097	73	14.35	3.107	59
17.76	2.525	57	16.40	2.728	24	14.90	2.995	16	15.79	2.830	26
18.80	2.414	8	1.690	2.649	10	15.80	2.828	12	16.10	2.777	8
			17.74	2.527	19	16.46	2.718	37	16.45	2.720	18
			18.90	2.377	9	16.92	2.646	14	16.88	2.652	8
			19.87	2.266	9	17.80	2.519	91	17.78	2.522	13
			20.20	2.230	10	18.83	2.386	12	18.95	2.371	11
						18.93	2.374	12	20.22	2.228	11
						19.24	2.337	8			
						20.03	2.248	29			
						20.44	2.205	13			

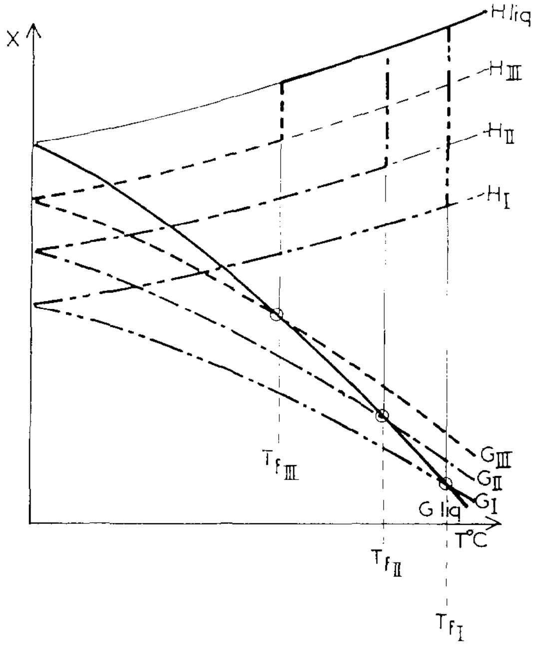


Fig. 5. Schematic energy–temperature diagram of polymorphic modifications **I**, **II** and **III**.

The second behavioural pattern involved all the other polymorphs which crystallized when melted and cooled rapidly. This behaviour was closer to that observed in a previous study of molecules in the same series with a slightly hindering substituent on the aromatic nucleus [2]. Note that substitutions that involve important steric groups induce the formation of glassy or amorphic solids.

Thus, the results for form **V** cannot be explained by steric hindrance or by a methyl group mesomeric effect on behaviour, which should have been identical in all forms. Nor did the results seem to be due to the formation of open dimers, because there was no significant shift in the frequency of the ν(OH) spectra, in comparison with other compounds in the same series [1,2].

It was instructive to compare infrared spectra frequencies for all of these forms with those of 3-*para*-thioanisoyl-1,2,2-trimethyl cyclopentane carboxylic acid polymorphs [1] whose structures were determined previously [3,4]. These comparisons showed that forms **IV**, **VI** and **VII** seemed to result from dimer formation with adjacent molecules, through associations with carboxylic groups of identical CO bond lengths [3]. They are transformed by heating to form **II**, where dimers were obtained by associations between classical carboxylic groups [4].

The transformation of **V** into **III** seemed quite different. Indeed, it was accompanied by an 18 cm^{-1} decrease in the γ_{AC}(OH) bending vibrations and by a $2\,\mathrm{cm}^{-1}$ decrease in the $\nu_{\mathrm{CE}}(\mathrm{C{=}O})$ frequency, whereas the $\nu_{\mathrm{AC}}(\mathrm{C{=}O})$ valence vibration frequency increased by $7\,\mathrm{cm}^{-1}$.

These variations allowed us to determine the characteristic frequencies of form **I** and indicated substantially different associations for forms **I** and **III**, with the carbonyl of the carboxylic group being less implicated than previously noted. This clearly suggests that the structures of these two forms include bonds between the hydroxyl of the carboxylic group of one molecule with the ketone carbonyls of another molecule, as often observed with ketonic acids [10], which are repeated infinitely to yield a chain.

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