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Thermal phase transitions of solid chiral *N*,*N*′-carbonyl-bis-(L-amino acids) and their methyl and benzyl esters

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Abstract

Compounds derived from different *N*,*N*′-carbonyl-bis-(L-amino acids) and their methyl and benzyl esters were synthesized and characterized by elemental analysis, infrared and nuclear magnetic resonance. The amino acids used were valine, leucine, phenylglycine and phenylalanine. All compounds revealed complex thermal behaviour as proved by differential scanning calorimetry, X-ray powder diffractometry and optical birefringence observation by polarizing microscope. Above isotropization temperature *N*,*N*′-carbonyl-bis-(L-amino acids) decomposed. The number and kinds of thermal phase transitions of investigated esters vary from a simple phase transition and melting to a complex polymorphism, and strongly depends on molecular structure. One to four phase transitions have been observed upon heating. Phase transition temperatures showed considerable variation with choice of the supstituent on symmetric carbons and therminal carboxylic groups. The results are discussed in terms of the architecture of investigated molecules that hinder mesomorphism.

Keywords: Phase transition; Polymorphism; *N*,*N*′-Carbonyl-bis-(L-amino acid); Methyl ester; Benzyl ester

1. Introduction

The phenomenon of polymorphism and mesomorphism is of considerable interest in the field of organic solid-state chemistry [1–6]. The understanding of relationship between crystal structure and thermal properties at molecular level is of importance for designing an organic compound for specific application. In addition, the gelation phenomenon and its supramolecular nature exhibited by low molecular weight organic compounds have recently attracted considerable attention. Numerous potential applications of gels as new "soft" materials are foreseen, for example, designing slow drug delivery systems, development of sensing devices or hardeners of liquid waste materials.

Recently, we have reported on synthesis and gelation properties of a versatile group of bis-(amino acid or amino alcohol)oxalamide gelators possessing a strongly hydrogen bonding and self-complementary oxalamide units [7]. As a part of our interest on polymorphism of amino acid ureido derivatives, and a systematic study of the gelator structure–properties relationship, we have prepared a series of *N*,*N*′-carbonyl-bis-(L-amino acids) derivatives incorporating leucine, valine, phenylalanine and phenylglycine (Scheme 1). It was found that such replacement of oxalamide with urea type of bridge lack any gelation properties. Generally, carbonyl-bis-(amino acid esters) showed phase transitions from solid to isotropic liquid phases, whereas some of them exhibited liquid crystalline, LC, behaviour prior to the isotropization [8,9]. The intermolecular hydrogen bonds between structural units are responsible for gelation and in some cases for the orientational ordering in liquid crystalline phases [10–14]. The symmetrical *N*,*N*′-disubstituted urea moiety has been often used in the synthesis of linear supramolecular polymers maintained by hydrogen bonds [15]. Aromatic ureas with multilayer structure of metal complexes might find application in the materials research, medicine and supramolecular chemistry [16]. The compounds derived from naturally occurring amino acids [9,10] and their alkyl esters [17–19] are used as chiral dopants to induce formation of lyotropic nematics and cholesteric phases. The sense and magnitude of the induced helical twist has been found to show a concentration dependent distribution of cis and trans molecular rotamers. The addition or

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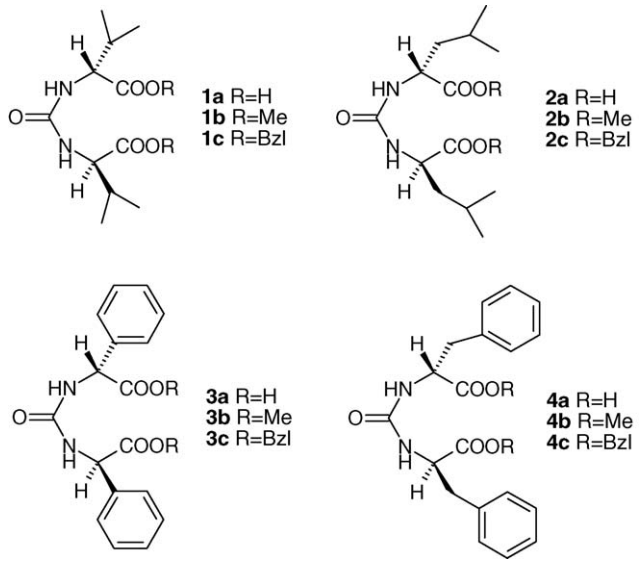

Scheme 1. The scheme of *N,N′*-carbonyl-bis-(L-amino acids), R = H (a), their methyl (R = Me) (b) and benzyl esters (R = Bzl) (c); accordingly the genuine amino acids: valine (group **1**), leucine (**2**), phenylglycine (**3**) and phenylalanine (**4**).

removal of even one CH_2 group in terminal chain can dramatically alter the phase types. The phase transition temperatures show an odd–even effect of the number of methylene units [20]. A novel kind of nematic liquid crystalline poly(urea-esters) has been obtained [21] with significant effect of monomer composition on melting point of polyesters.

In this paper we describe the synthesis and thermal behaviour of the organic solid crystalline phases of carbonyl-bis-(L-amino acids) derived from leucine, valine, phenylalanine and phenylglicine, and their methyl and benzyl esters. The discussion of the results is focused on the relationship between the structure and thermal behaviour of compounds.

2. Experimental

2.1. Materials, preparation and characterization of the compounds

Reagents were purchased from Aldrich, Fluka, Kemika and Merck, and were used without further purification. All solvents were purified and dried according to standard procedures. The reactions were monitored by thin-layer chromatography (t.l.c.) on Merck Kieselgel HF254 plastic sheets and spots were made visible using a UV lamp (254 nm) or I_2 vapours. Prepared compounds were purified chromatographically by preparative t.l.c. using silica gel *Merck HF*$_{254}$ and by column chromatography using silica 0.063–0.2 mm (Merck). Reaction yields are not optimised.

All *N,N′*-carbonyl-bis-(L-amino acids derivatives) were prepared as described at general procedures [8,9,22–25] and their purity was checked by elemental and spectral analysis. The compounds **1b** [8,9], **1c** [8], **2b** [22], **2c** [23], **3b** [23,24], **4a** [22], **4b** [22,25] and **4c** [25] (Scheme 1), were described previously, but most of them were not spectroscopically characterized. Therefore, we characterized spectroscopically some missing *N,N′*-carbonyl-bis-(L-amino acids) (**1a**–**3a**), *N,N′*-carbonyl-bis-(L-amino acid metyl esters) (**1b**, **3b** and **4b**) and *N,N′*-carbonyl-bis-(L-amino acid benzyl estzers) (**1c**–**4c**).

*2.1.1. N,N′-Carbonyl-bis-(L-valine acid) (**1a**)*

$[\alpha]_D$ + 16 (c 0.77, MeOH); (found: C, 50.82; H, 7.88; N, 10.65; $C_{11}H_{20}N_2O_5$ requires C, 50.76; H, 7.74; N, 10.76%); IR (KBr) ν_{max} (cm^{-1}) 3330, 3300, 1697, 1629, 1558 and 1550; ^{1}H NMR (300 MHz; DMSO-d_6M) δ_H (ppm) 0.81 and 0.84 (6 H each, 2 d, *J* 6.8, $CH_{3(\gamma)}$), 1.60–2.05 (2 H, m, CH_β), 3.98 (2 H, dd, *J* 4.7 and 9.0 CH_α), 6.28 (2 H, d, *J* 9.0, NH), 12.46 (2 H, s br, COOH); ^{13}C NMR (75.5 MHz; DMSO-d_6) δ_C (ppm) 17.7 and 19.3 ($CH_{3(\gamma)}$), 30.4 (CH_β), 57.5 (CH_α), 157.5 (CONH) and 174.1 (COOH).

*2.1.2. N,N′-Carbonyl-bis-(L-leucine acid) (**2a**)*

$[\alpha]_D$ − 7.1 (c 0.84 in acetone); (found: C, 54.22; H, 8.15; N, 9.71; $C_{13}H_{24}N_2O_5$ requires C, 54.15; H, 8.39; N, 9.72%); IR (KBr) ν_{max} (cm^{-1}) 3390 br, 1723, 1640 and 1566; ^{1}H NMR (300 MHz; acetone-d_6) δ_H (ppm) 0.92 and 0.93 (6 H each, 2 d, *J* 6.6, $CH_{3(\delta)}$), 1.48–1.84 (6 H, m, $CH_{2(\beta)}$ and CH_γ), 4.38 (2 H, dt, *J* 5.2 and 8.5, CH_α), 6.00 (2 H, d, *J* 8.5, NH) and 9.65 (2 H, br s, COOH); ^{13}C NMR (75.5 MHz; acetone-d_6) δ_C (ppm) 213, 22.5 ($CH_{3(\delta)}$), 24.5 (CH_γ), 41.4 ($CH_{2(\beta)}$), 51.5 (CH_α), 158.6 (CONH) and 175.0 (COOH).

*2.1.3. N,N′-Carbonyl-bis-(L-phenylglycine acid) (**3a**)*

$[\alpha]_D$ + 50 (c 0.5 in 96% EtOH); (found: C, 24.30; H, 2.73; N, 18.89; $C_3H_4N_2O_5$ requires C, 24.33; H, 2.72; N, 18.92%); IR (KBr) ν_{max} (cm^{-1}) 3350, 3066 br, 1718, 1676, 1636, 1587 and 1570; ^{1}H NMR (300 MHz; acetone-d_6) δ_H (ppm) 5.43 (2 H, d, *J* 8.1 CH_α), 6.90 (2 H, d, *J* 8.1, NH), 7.25–7.48 (10 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; acetone-d_6) δ_C (ppm) 57.1 (CH_α), 127.3, 127.9, 128.6, 138.6(C_{arom}), 156.8 (CONH) and 172.5 (COOH).

*2.1.4. N,N′-Carbonyl-bis-(L-valine acid methyl ester) (**1b**)*

$[\alpha]_D$ − 8 (c 1 in CH_2Cl_2–MeOH, 2:3); IR (KBr) ν_{max} (cm^{-1}) 3338, 1742, 1632 and 1572; ^{1}H NMR (300 MHz; acetone-d_6) δ_H (ppm) 0.89 and 0.95 (6 H each, 2 d, *J* 6.9, $CH_{3(\gamma)}$), 2.05–2.15 (2 H, m, CH_β), 3.76 (6 H, s, $CH_{3(OMe)}$), 4.46–4.41 (2 H, m, CH_α), 5.21 (2 H, s br, NH); ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 17.4 and 18.6 ($CH_{3(\gamma)}$), 31.1 (CH_β), 51.8 ($CH_{3(OMe)}$), 57.6 (CH_α), 157.5 (CONH) and 173.9 (COOMe).

*2.1.5. N,N′-Carbonyl-bis-(L-phenylglycine acid methyl ester) (**3b**)*

$[\alpha]_D$ + 158 (c 1 in CH_2Cl_2–MeOH, 2:3); IR (KBr) ν_{max} (cm^{-1}) 3854, 1737, 1637 and 1567; ^{1}H NMR (300 MHz; $CDCl_3$) δ_H (ppm) 3.67 (6 H, s, $CH_{3(OMe)}$), 5.48 (2 H, d, *J* 7.1, CH_α), 6.00 (2 H, d, *J* 7.1, NH) and 7.32–7.54 (10 H, m, H_{arom}), ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 52.5 ($CH_{3(OMe)}$), 56.8 (CH_α), 126.9, 128.0, 128.6, 137.1 (C_{arom}), 155.7 (CONH) and 172.5 (COOMe).

*2.1.6. N,N′-Carbonyl-bis-(L-phenylalanine acid methyl ester) (**4b**)*

$[\alpha]_D$ + 44 (c 1 in CH_2Cl_2–MeOH, 2:3); IR (KBr) ν_{max} (cm^{-1}) 3851, 1742, 1715, 1634 and 1578; ^1H NMR (300 MHz; $CDCl_3$) δ_H (ppm) 2.99 (4 H, d, *J* 5.8, $CH_{2(\beta)}$), 3.61 (6 H, s, $CH_{3(OMe)}$), 4.79 (2 H, dt, *J* 5.8 and 8.2, CH_α), 5.38 (2 H, d, *J* 8.2, NH), 7.05–7.32 (10 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 38.7 ($CH_{2(\beta)}$), 52.0 ($CH_{3(OMe)}$), 53.8 (CH_α), 126.7, 128.2, 129.2, 136.1 (C_{arom}), 156.3 (CONH) and 173.3 (COOMe).

*2.1.7. N,N′-Carbonyl-bis-(L-valine acid benzyl ester) (**1c**)*

$[\alpha]_D$ − 4 (c 1 in CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}) 3310, 1730, 1617 and 1565; ^1H NMR (300 MHz; $CDCl_3$) δ_H (ppm) 0.79 and 0.92 (6 H each, d, *J* 6.7, $CH_{3(\gamma)}$), 2.06–2.18 (2 H, m, CH_β), 4.52–4.58 (2 H, m, CH_α), 5.12 and 5.25 (2 H each, 2 d, *J* 12.4, $CH_{2(OBn)}$), 7.24–7.46 (10 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 17.3 and 18.9 ($CH_{3(\gamma)}$), 31.4 (CH_β), 57.7 (CH_α), 66.9 ($CH_{2(OBn)}$), 128.1, 128.4, 135.2 (C_{arom}), 157.4 (CONH) and 173.5 (COOBn).

*2.1.8. N,N′-Carbonyl-bis-(L-leucine acid benzyl ester) (**2c**)*

$[\alpha]_D$ − 9 (c 1 in CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}) 3560, 3350, 1748, 1730, 1709, 1660, 1649, 1580 br and 1545; ^1H NMR (300 MHz; $CDCl_3$) δ_H (ppm) 0.87 (6 H, d, *J* 5.4, $CH_{3(\delta)}$), 0.89 (6 H, d, *J* 6.1, $CH_{3(\delta)}$), 1.41–1.70 (6 H, m, $CH_{2(\beta)}$ and CH_γ), 4.56 (2 H, dt, *J* 5.2 and 8.6, CH_α), 5.12 and 518 (2 H each, 2 d, *J* 12.4, $CH_{2(OBn)}$), 5.48 (2 H, d, *J* 8.6, NH) and 7.22–7.44 (10 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 21.7 and 22.4 ($CH_{3(\delta)}$), 24.4 (CH_γ), 41.9 ($CH_{2(\beta)}$), 51.4 (CH_α), 66.7 ($CH_{2(OBn)}$), 127.9, 128.1, 128.4, 135.3 (C_{arom}), 157.0 (CONH) and 174.5 (COOBn).

*2.1.9. N,N′-Carbonyl-bis-(L-phenylglycine acid benzyl ester) (**3c**)*

$[\alpha]_D$ + 70 (c 0.5 in CH_2Cl_2); (found: C, 70.89; H, 5.50; N, 5.26; $C_{31}H_{28}N_2O_5{\cdot}H_2O$ requires C, 70.70; H, 5.74; N, 5.32%); IR (KBr) ν_{max} (cm^{-1}) 3354, 1736, 1637, 1590 and 1567; ^1H NMR (300 MHz; d_6-$CDCl_3$) δ_H (ppm) 5.11 (4 H, s, $CH_{2(OBn)}$), 5.56 (2 H, d, *J* 7.3 CH_α), 6.03 (2 H, d, *J* 7.3, NH) and 7.25–7.28 (20 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; $CDCl_3$) δ_C (ppm) 57.1 (CH_α), 67.3 ($CH_{2(OBn)}$), 127.0, 127.7, 128.2, 128.3, 128.7, 135.0, 137.1 (C_{arom}), 155.4 (CONH) and 171.5 (COOBn).

*2.1.10. N,N′-Carbonyl-bis-(L-phenylalanine acid benzyl ester) (**4c**)*

$[\alpha]_D$ + 14 (c 1 in CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}) 3470,1731, 1723,1627 and 1563; ^1H NMR (300 MHz; $CDCl_3$) δ_H (ppm) 3.00 (4 H, d, *J* 5.6, $CH_{2(\beta)}$), 4.85 (2 H, dt, *J* 5.6 and 8.3, CH_α), 4.97 and 5.11 (2 H each, 2 d, *J* 12.1, $CH_{2(OBn)}$), 5.19 (2 H, d, *J* 8.3, NH), 6.94–7.39 (20 H, m, H_{arom}); ^{13}C NMR (75.5 MHz; $CDCl_3$), δ_C (ppm) 53.7 (CH_α), 67.0 ($CH_{2(OBn)}$), 126.8, 128.4, 128.5, 129.4, 135.1, 135.9 (C_{arom}), 156.1 (CONH) and 172.7 (COOBn).

2.2. Measurements

Elemental analyses, CHN, were performed on a Perkin-Elmer Analyser PE 2400 Series 2. Optical rotations were measured on an Optical Activity AA-10 Automatic Polarimeter in a 1 dm cell using the wavelength of 589.3 nm, concentrations were given in g/100 ml. IR spectra were recorded in KBr pallets on Perkin-Elmer 297 spectrometer and Perkin-Elmer Spectrum RX-1 FT-IR spectrophotometer, wave numbers (ν) are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6, acetone-d_6 or $CDCl_3$ on a Varian XL-Gemini 300 (300/75) spectrometer operating at 300.07 for the ^1H and 75.46 MHz for the ^{13}C resonance with tetramethylsylane (TMS) as an internal standard. Chemical shifts (δ) were given in ppm, coupling constants (*J*) in Hz, and spin multiplicities as s (singlet), d (doublet), t (triplet), q (quadruplet) and m (multiplet).

Thermal properties were examined by thermogravimetric analysis, TGA, with Mettler TA 4000 System in air atmosphere, and differential scanning calorimetry, DSC, with Perkin-Elmer DSC-7 calorimeter in N_2 atmosphere (Messer, 2×10^5 Pa). The solid sample was placed in an aluminium capsule, heated and cooled at the rate of 5 K min^{-1}. All results were taken from the first heating and cooling run, detecting the level of enthalpy change that is associated with a respective phase transition. The transition enthalpy, ΔH (kJ mol^{-1}), was determined from the peak area of the DSC thermogram. The transition entropy, ΔS (kJ mol^{-1} K^{-1}), was calculated with the equation $\Delta S = \Delta H/T$, where *T* was the transition temperature corresponding to the DSC maximum. The thermodynamic data were mean values of several independent measurements carried out on different samples. The investigation by TGA pointed to thermal instability, i.e. successive decomposition at the temperature of isotropization, T_i, of *N,N′*-carbonyl-bis-(amino acids) (**1a**–**4a**); *N,N′*-carbonyl-bis-(L-leucine acid methyl/meso and benzyl esters) (**meso-2b** and **2c**); and *N,N′*-carbonyl-bis-(L-phenylglycine acid methyl ester) (**3b**).

Diffraction patterns have been obtained by an automatic wideangle X-ray powder diffractometer, XRD, with a high-temperature attachment (Philips MPD 1880, with monochromatized Cu Kα radiation and proportional counter). The patterns were recorded at room temperature, RT_I, at higher temperatures between points of phase transitions in accordance with the DSC curves, and again at room temperature, RT_{II}, after cooling. The samples were heated and cooled at the rate of 5 K min^{-1}, and at chosen temperatures the samples were left 15 min for stabilization. The acquisition time for each diffractogram was ca. 20 min and during each exposure the temperature change was ±1.5%.

A Carl-Zeiss optical polarizing microscope with a hot stage and digital Olympus camera was used for morphology and texture investigations.

3. Results and discussion

The general structures of investigated *N,N′*-carbonyl-bis-(L-amino acids) and their esters are shown in Scheme 1.

The first and the third group differ from the second and the fourth ones in one methylene (CH_2) unit on each side, whereas the first two groups differ from the last two by the short branched alkane (isopropyl and isobutyl) replaced by phenyl and benzyl groups, respectively. Each compound has two asymmetric centres of the same configuration.

3.1. Analysis of thermal properties of different amino acids and their esters

The DSC thermograms all of investigated compounds revealed that the number and types of thermal phase transitions varied by melting from a simple phase transition to a complex polymorphism. All transitions are in the heating cycle endothermic and exothermic in the cooling cycle. Typical thermograms of *N*,*N*′-carbonyl-bis-(L-valine acid methyl ester) (**1b**) and *N*,*N*′-carbonyl-bis-(L-leucine acid methyl ester) (**2b**) are illustrated in Fig. 1A and B. In the same compound, there might be more than one state and each being a stable phase within a particular range of temperature. The temperature corresponding to the isotropic phase transition (the last transitions in the heating cycle) has been denoted as T_i. The endothermic transitions below T_i corresponded to the polymorphic transitions and melting, T_m. It is well known that the formation of liquid crystalline phase, LC, advances between T_m and T_i in the heating scan, and between the temperatures of deisotropization, T_d, and temperatures of crystallization, T_c, in the cooling run [1,2,18]. In Tables 1–4 for acids and their esters their phase transition parameters, i.e. transition temperatures, changes in the enthalpy and entropy derived from the DSC heating and cooling scans are listed. The compounds which did not decompose upon heating, exhibited temperature hysteresis. The T_c was shifted down for >50 K (group **1**), >20 K (**2**) and >60 K (**3** and **4**), respectively. Almost all peaks in the heating cycle showed their corresponding peaks in the cooling cycle. The exceptions were the compounds which decomposed upon heating (**1a**, **2a**, **meso-2b**, **2c**, **3a**, **3b** and **4a**), and esters (**1e**, **2b**, **3c** and **4c**) showing lack of one exothermic peak. On the contrary, their racemic (**rac-2b**) and meso forms (**meso-3c**) exhibited one peak in excess.

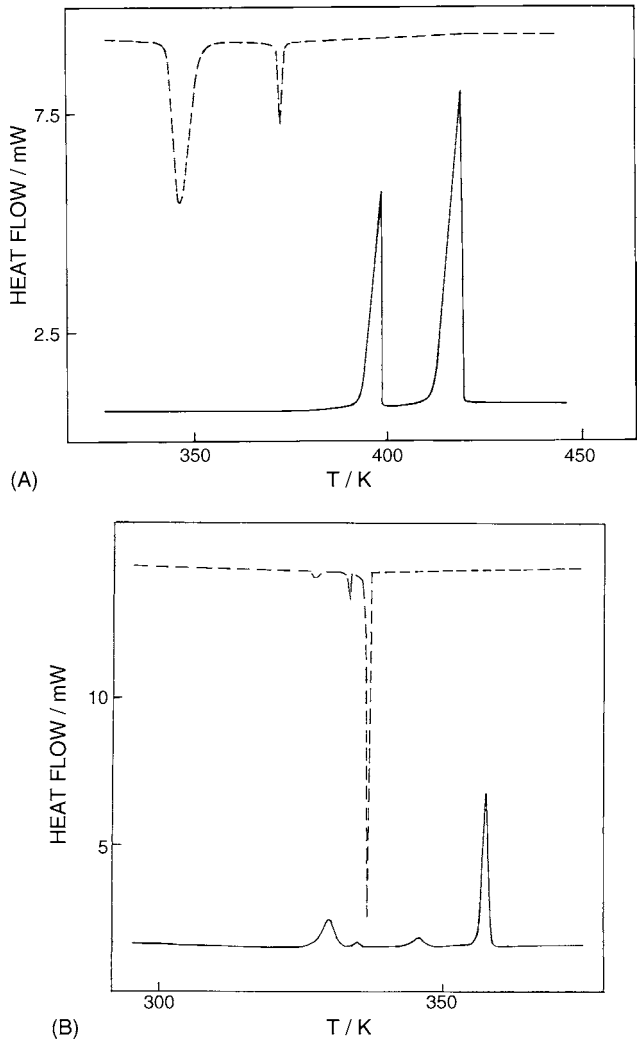

Fig. 1. Typical thermograms of (A) *N*,*N*′-carbonyl-bis-(L-valine acid methyl ester) (**1b**) and (B) *N*,*N*′-carbonyl-bis-(L-leucine acid methyl ester) (**2b**), obtained by differential scanning calorimetry during heating (endothermic transitions, full lines) and cooling runs (exothermic transitions, dashed lines).

3.1.1. N,N′-carbonyl-bis-(L-valine acid and esters)

The heating scan of *N*,*N*′-carbonyl-bis-(L-valine acid) (**1a**), had only one endothermic transition (Table 1). Microscopic observation showed that this peak related to the transition from the crystalline to the isotropic liquid state and to the beginning of decomposition.

Table 1 clearly shows that the esterification of the *N*,*N*′-carbonyl-bis-(L-valine acid) (**1a**) and the increase in number of C-atoms in the ester chains leads to additional phase transitions, and to the decrease of isotropization temperatures. The minimum of first transition temperature T_1 values was observed for *N*,*N*′-carbonyl-bis-(L-valine acid ethyl ester) (**1d**). The corresponding enthalpies and entropies changes showed that methyl ester was organized best, whereas benzyl ester proved to be a most disorganized phase.

3.1.2. N,N′-carbonyl-bis-(L-leucine acid and esters)

As compared to valine derivatives, leucine derivatives (group **2**) exhibited similar changes of transition temperatures, enthalpies and entropies (Table 2). Prior to isotropization the **2b** compounds exhibited greater number of phase transitions. The lowest values of T_i and T_c for **2b** seems to be optimal for the LC phase formation. The behaviour of the group **2** derivatives with regard to first transition temperature T_1 is not continuous. The enthalpy and entropy changes slightly decreased from acid to methyl ester and then continuously increased from isopropyl to benzyl ester. Generally, racemic compounds melt at higher temperatures than their enantiomeric analogues. Their more solid thermodynamic stability originates from an increased structural compactness and symmetry.

3.1.3. N,N′-carbonyl-bis-(L-phenylglycine acid and esters)

N,*N*′-carbonyl-bis-(L-phenylglycine acid) (**3a**) and corresponding esters (**3b** and **3c**) exhibited an increase in T_1 upon esterification (Table 3). *N*,*N*′-Carbonyl-bis-(L-phenylglycine acid methyl ester) (**3b**) showed the minimum of T_i value, but

Table 1
Transition temperatures, T, enthalpies, ΔH and entropies, ΔS, for *N*,*N*′-carbonyl-bis-(L-valine acid and esters)

Compound	Heating			Cooling		
	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})
Acid **1a**	410	19.5	47.7	Decomposition at T_i		
Methyl ester **1b**	382	3.1	8.0	331	−5.6	−16.9
	415	7.2	17.4	366	−2.2	−6.0
Ethyl[a] ester **1d**[a]	361	1.8	5.1	–	–	–
	388	8.4	21.6	–	–	–
Isopropyl ester **1e**[a]	364	9.4	25.9	369	−1.7	−4.6
	372	0.4	1.1	373	−5.5	−14.8
	382	6.5	17.0			
tert-Butyl[a] ester **1f**[a]	427	(broad transition)		398	−13.7	−34.4
	–	–	–	402	−6.4	−15.9
Benzyl ester **1c**	384	29.3	76.3	321	−18.2	−56.6

[a] Results recalculated according to Ref. [9].

Table 2
Transition temperatures, T, enthalpies, ΔH and entropies, ΔS, for *N*,*N*′-carbonyl-bis-(L-leucine acid and esters)

Compound	Heating			Cooling		
	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})
Acid **2a**	411	26.4	64.3	Decomposition at T_i		
Methyl ester **2b**	330	4.7	14.3	328	−0.01	−0.03
	335	0.1	0.2	333	−0.8	−2.2
	346	1.4	4.1	337	−13.3	−39.4
	357	12.6	35.3	–	–	–
Methyl ester/racemic **rac-2b**	396	32.4	81.9	346	−20.8	−60.2
	–	–	–	372	−2.7	−7.4
Methyl ester/meso **meso-2b**	353	20.1	56.9	Decomposition at T_i		
Isopropyl ester (D) **2d**[a]	328	22.51	68.6	–	–	–
	383	2.3	5.9	–	–	–
Benzyl ester **2c**	365	58.4	168.3	Decomposition at T_i		

[a] Results recalculated according to Ref. [9].

at this temperature the degradation started for both the acid and its methyl ester. The benzyl ester showed several phase transitions prior to isotropization, and the small endothermic peak indicated pre-melting [26]. The cooling run was characterized by an expressed temperature hysteresis and a disappearance of one of the transitions. Regarding either the number of polymorphs or the temperatures of transitions, the **3c** and **meso-3c** compounds differ from each other signifficantly.

The investigated compounds **2b**, **rac-2b** and **meso-2b** (Table 2), and also the **3c** and **meso-3c** (Table 3) show completely

Table 3
Transition temperatures, T, enthalpies, ΔH and entropies, ΔS, for *N*,*N*′-carbonyl-bis-(L-phenylglycine acid and esters)

Compound	Heating			Cooling		
	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1}K^{-1})	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1}K^{-1})
Acid **3a**	402	5.1	12.8	Decomposition at T_i		
	455	43.0	94.6			
Methyl ester **3b**	428	54.5	127.3	Decomposition at T_i		
Benzyl ester **3c**	420	0.3	0.8	348	−3.8	−11.0
	450	28.1	62.4	377	−3.8	−9.9
	456	0.1	0.2	407	−9.5	−23.3
	470	6.1	12.9	–	–	–
Benzyl ester/meso **meso-3c**	485	63.8	131.6	367	−2.6	−7.1
	–	–	–	400	−11.7	−29.3

Table 4
Transition temperatures, T, enthalpies, ΔH and entropies, ΔS, for N,N'-carbonyl-bis-(L-phenylalanine acid and esters)

Compound	Heating			Cooling		
	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1}K^{-1})	T (K)	ΔH (kJ mol^{-1})	ΔS (J mol^{-1}K^{-1})
Acid **4a**	337	4.3	12.8	Decomposition at T_i		
	370	23.8	64.3			
	374	13.9	37.2			
	456	54.8	120.3			
Methyl ester **4b**	403	1.2	3.0	351	−0.8	−2.4
	434	42.4	97.7	362	−26.1	−72.0
Benzyl ester **4c**	428	32.0	74.9	374	−40.3	−107.9
	434	26.4	60.7	–	–	–

different thermodynamic parameters. The highest values of T_1, T_i and T_c were observed for racemic methyl ester, and the entropy values in the heating and cooling runs indicated this form as the most disorganized. Although the data for racemic N,N'-carbonyl-bis-(phenylglycine acid benzyl ester) are missing, it seems that the T_1, T_c and T_m values increase from the L,L to meso forms, and that the most organized phase is the L,L benzyl ester.

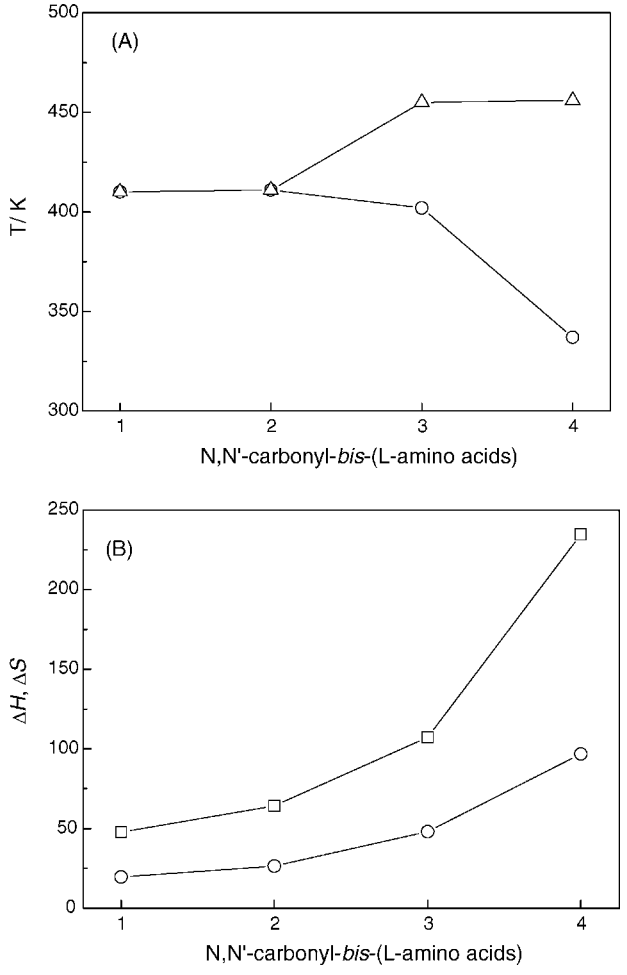

Fig. 2. (A) The T_1 (open circle) and T_i (open up triangle); and (B) ΔH (kJ mol^{-1}) (open circle) and ΔS (J K^{-1} mol^{-1}) (open square) vs. the different investigated N,N'-carbonyl-bis-(L-amino acids), the **1a**–**4a** (1–4) compounds.

3.1.4. N,N′-carbonyl-bis-(L-phenylalanine acid and esters)

N,N'-carbonyl-bis-(L-phenylalanine acid and esters) (group **4**) exhibited a reduced number of phase transitions upon

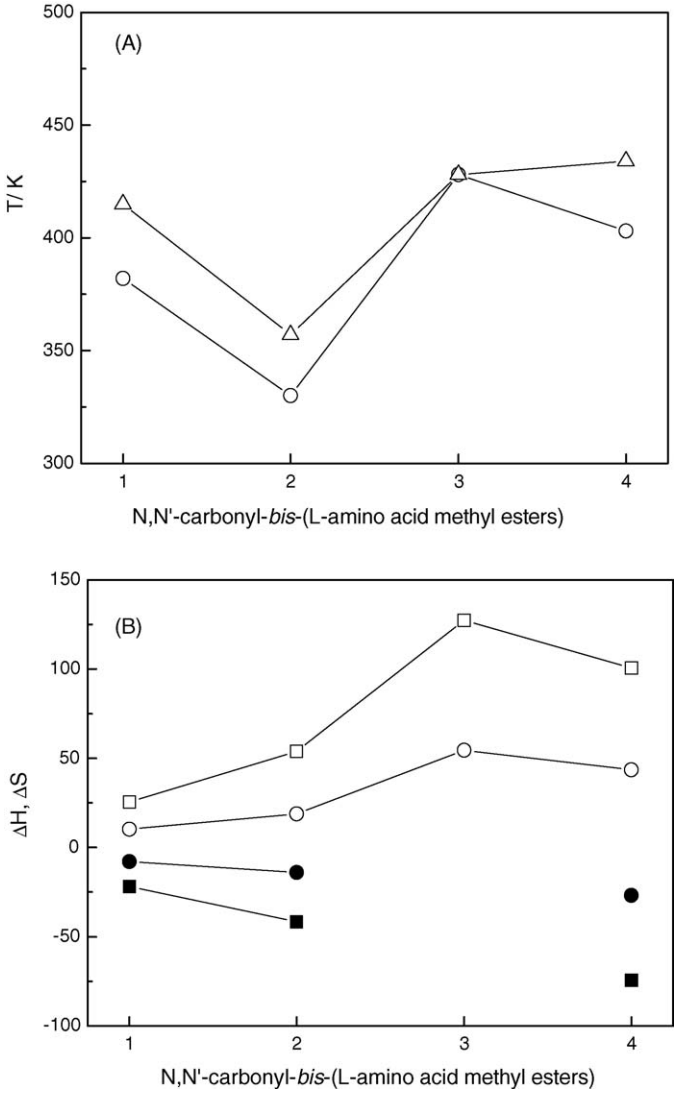

Fig. 3. (A) T_1 (open circle), T_i (open up triangle); (B) ΔH (kJ mol^{-1}) (open circle in the heating run, and solid circle in the cooling run) and ΔS (J K^{-1} mol^{-1}) (open square in the heating run, and solid square in the cooling run) vs. the different N,N'-carbonyl-bis-(L-amino acid methyl esters), the **1b**–**4b** (1–4) compounds.

esterification, as well a continual lessening of the temperature interval between first transition temperature, T_1, and T_i (Table 4). The methyl and benzyl esters showed the enhanced T_1 and T_c values, and the declined T_i values. In the heating and cooling cycle, among all phases the methyl ester phase was best organized.

The influence of the hydrocarbon chain length on the phase transitions of *N,N′*-carbonyl-bis-(L-amino acids) and their methyl and benzyl esters is not as simple as for normal paraffin, sodium alkyl sulfates [27], alkylammonium halogenides [28,29], and symmetric or asymmetric catanionic surfactants [1,3,5,6,27–29]. The above compounds showed linear dependence of the changes in transition temperatures, enthalpies and entropies upon the number of carbon atoms in the alkyl chains. The calculated enthalpy increment per methylene group for the acids **2a** and **1a** is 3.5 kJ mol^{-1}, for the methyl esters **2b** and **1b** is 4.3 kJ mol^{-1} in the heating run and 3.2 kJ mol^{-1} in the cooling run, and for the isopropyl esters **2d** and **1e** is 4.3 kJ mol^{-1}. The reasonable enthalpy values per methylene group inside the same group of compounds were found only for couples **1e** and **1d**, carbonyl-bis-(L-valine acid isopropyl and ethyl ester); **3a** and **3b**, carbonyl-bis-(L-phenylglycine acid and methyl ester); in amounts of 3.1 and 3.2 kJ mol^{-1}, respectively. All these values lower than 4.1 kJ mol^{-1} per methylene group point to the unconventional packing [30].

A subtle structural changes involved in the LC phase transitions are characterized by relatively small enthalpy changes. Typically, the melting transitions from a crystalline solid to a liquid crystal phase or to the isotropic liquid phase generates an enthalpy change of around 30–50 kJ mol^{-1}, whereas transition from smectic mesophase to isotropic liquid of about 6 kJ mol^{-1}. The enthalpy changes of transitions between different LC phases can be extremely small (<1 kJ mol^{-1}) [31]. The enthalpy changes of the last transitions into the isotropic liquids for the **1b**, **1d** and **1e** (Table 1), for the **2b** and **2d** (Table 2), and for the **3c** (Table 3), are in the cited ranges in the heating runs, pointed to the smectic LC phases.

3.1.5. *Analysis of thermal properties of different N,N′-carbonyl-bis-(L-amino acids)*

Comparing the *N,N′*-carbonyl-bis-(L-amino acids) (**1a**–**4a**) (Tables 1–4; Fig. 2), one might assume that the temperature of the first transition for valine and leucine derivatives is both the temperature of isotropization and decomposition. The number of phase transitions increased for phenylglycine to two, and for phenylalanine derivatives to four, whereas the last temperatures for aromatic derivatives are the decomposition temperatures. The values of the decomposition temperatures for 50 K higher than those of non-aromatic derivates suggested higher excitation requirements for higher homologues (**2a** and **4a** versus **1a** and **3a**) and aromatic homologues (**3a** and **4a** versus **1a** and **2a**). Upon an introduction of the aromatic group and an additional introduction of the methylene groups, the first transition temperatures lowered. The overall enthalpy and entropy changes were much higher than the values typical for the LC mesophases transition [32], thus, at the same time indicating an enhanced disorder of the investigated acids series.

3.1.6. *Analysis of thermal properties of different N,N′-carbonyl-bis-(L-amino acid methyl esters)*

A drop of the T_1 and T_i values (**1b**–**4b**, Tables 1–4; Fig. 3) was noticed for *N,N′*-carbonyl-bis-(L-amino acid methyl esters) by introduction of methylene unit in investigated non-aromatic and aromatic derivatives. In the heating run, the enthalpy and entropy changes of methyl esters of valine and leucine derivatives (**1b** and **2b**) were slightly increasing. The same values of aromatic derivatives (**3b** and **4b**) were higher showing a slight decrease. It was an indication that the introduction of methylene unit in non-aromatic methyl ester derivatives induced the formation of less organized structures by either heating ar cooling. The structures of atromatic methyl ester derivatives showed less order but their order improved upon an introduction of methylene unit.

3.1.7. *Analysis of thermal properties of different N,N′-carbonyl-bis-(L-amino acid benzyl esters)*

The higher temperatures of the different *N,N′*-carbonyl-bis-(L-amino acid benzyl esters) (**1c**–**4c**) transitions minimize the probability of the LC mesophases development (particularly

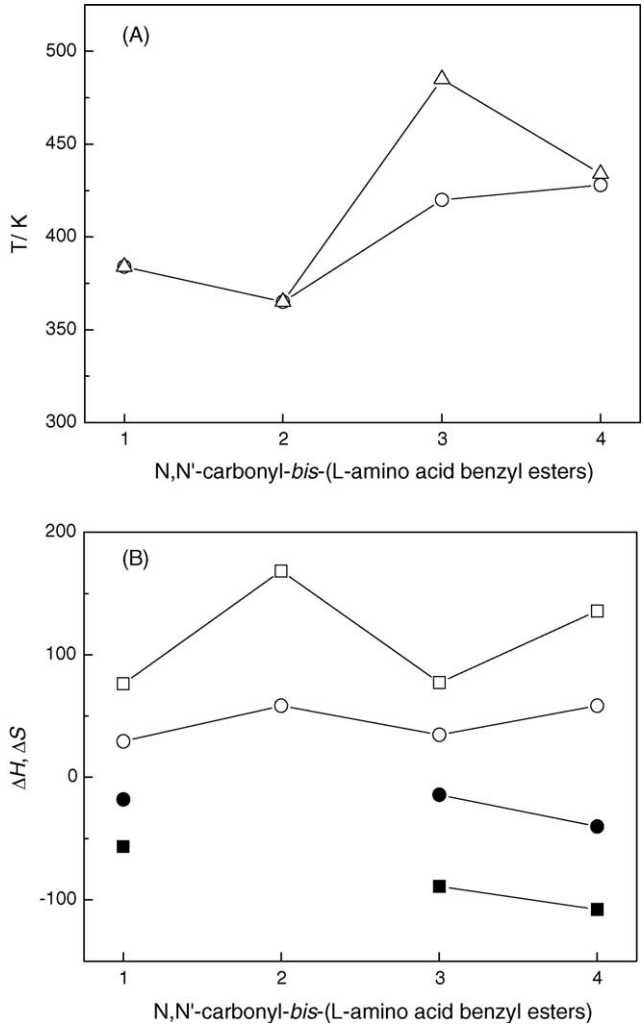

Fig. 4. (A) T_1 (open circle), T_i (open up triangle); (B) ΔH (kJ mol^{-1}) (open circle in the heating run, and solid circle in the cooling run) and ΔS (J K^{-1} mol^{-1}) (open square in the heating run, and solid square in the cooling run); vs. the different *N,N′*-carbonyl-bis-(L-amino acid benzyl esters), the **1c**–**4c** (1–4) compounds.

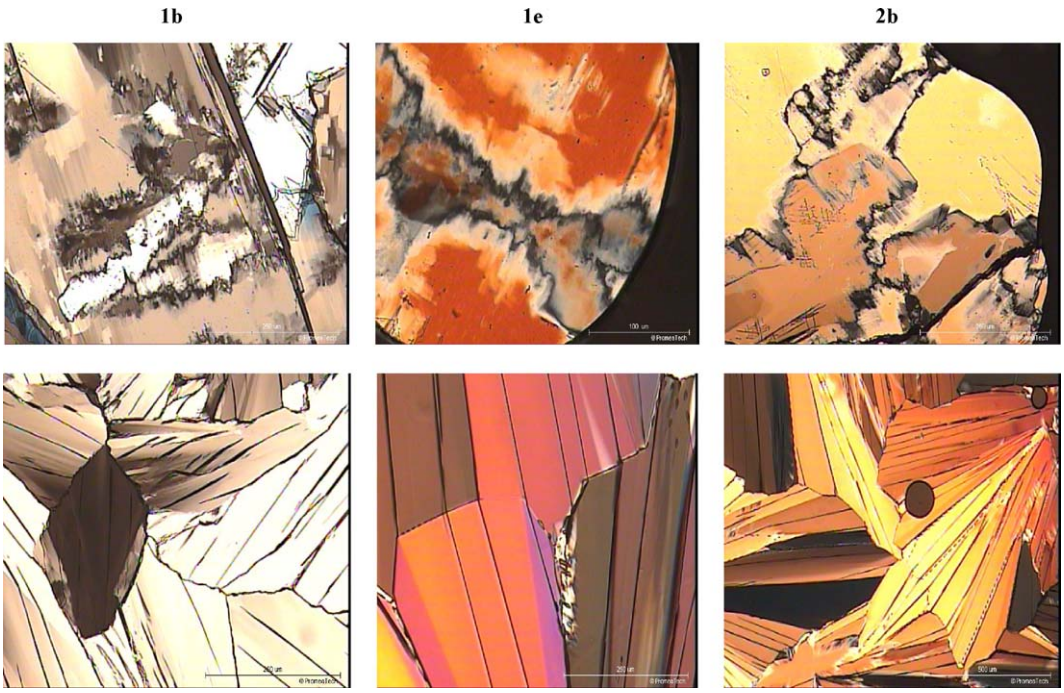

Fig. 5. The micrographs of the characteristic textures formed upon heating (upper part) and cooling (lower part) of the **1b**, **1e** and **2b**, as observed under crossed polarizers. The photographs of compounds are taken in the heating cycles at 403 K (**1b**), 378 K (**1e**) and 353 K (**2b**), respectively, and after isotropization in the cooling cycles at room temperature.

for the **3c** and **4c** compounds), even though the introduction of methylene group reduces the T_1 and T_i values of valine and leucine derivatives. The phenylglicine and phenylalanine derivatives showed an increase in the T_1 and a decrease in the T_i and T_c values upon an introduction of CH_2 unit (Fig. 4A). Further, the **1c**–**4c** compounds showed additionally more disorganized phases in the heating cycle after an introduction of one CH_2 unit to both non-aromatic and aromatic derivatives, as seen from the ΔS curve in Fig. 4B and in Tables 1–4.

3.2. Microphotographs of characteristic textures

The microphotographs of some characteristic textures formed upon heating and cooling of the examined compounds are illustrated in Fig. 5. The textures can be divided into three groups: the first one with a mosaic texture (**1b**, **1e** and **2b** in the heating run), the second one with spherulitic texture (**1b**, **1e**, **2b**, **1c**, **rac-2b**, **3c**, **meso-3c** and **4b**, all in the cooling run), both described in the literature as lamellar smectic mesophases [4,6,9,33]; and the third one with structured lancets or feather-like textures (**4c**). The temperature range over which the suspect mesomorphic behaviour has been observed in valine series decreased with an inrease in size of the ester group, in heating runs: from 33 K for methyl (**1b**) and 27 K for ethyl (**1d**) to 18 K for isopropyl ester (**1e**), and in cooling runs: 35 K for methyl (**1b**) and 4 K for isopropyl ester (**1e**) (Table 1).

3.3. X-ray analysis

The most interesting isotropic transitions of the compounds **1b**, **1d**, **1e**, **1f** and **2d** esters have been described in literature as "very probably smectic" based on their specific relatively small enthalpy changes and the polarizing microscope examinations during heating and cooling [9]. Due to literature data [9], and some similarities of ionic surfactant crystal smectic textures [5,6] with those observed in this work upon heating and cooling, the nature of phase transitions of **1b**, **1e**, **2b** and **3c** has been analysed by the XRD at different temperatures: at room temperature, RT_I, at characteristic temperatures during heating, after isotropization, and on cooling at RT_{II}. The characteristic parts of X-ray diffraction patterns taken during the heating cycles at chosen temperatures of 403 K (**1b**), 378 K (**1e**) and 353 K (**2b**) are shown in Fig. 6.

Generally, the amorphisation of almost the whole sample volume of the compounds **1b**, **1e**, **2b** and **3c** (not shown) has been noticed above the temperatures of isotropization, but no evidence of smectic phase has been noticed below T_i (Fig. 6). On cooling down to RT_{II} the crystallization with rather sharp diffraction lines has been observed. The XRD pattern differed from the initial pattern at RT_I, containing smaller number of diffraction lines indicating a higher symmetry. The XRD results lead to a conclusion that all the investigated compounds and their thermotropic polymorphs have typical crystal 3-D structures.

Some chiral molecules that generate the LC phases are very special and unusual. The necessary requirements for organic thermotropic liquid crystals are molecular structures shaped favourably with good lateral attractions, relatively low melting points and/or symmetrical molecular structures. The symmetrical architecture of *N*,*N*′-carbonyl-bis-(amino acids and esters) molecules includes two strong polar groups near the centre and two along the molecular axis, which all together enhance the liquid crystallinity. The compounds have polarizable, planar and

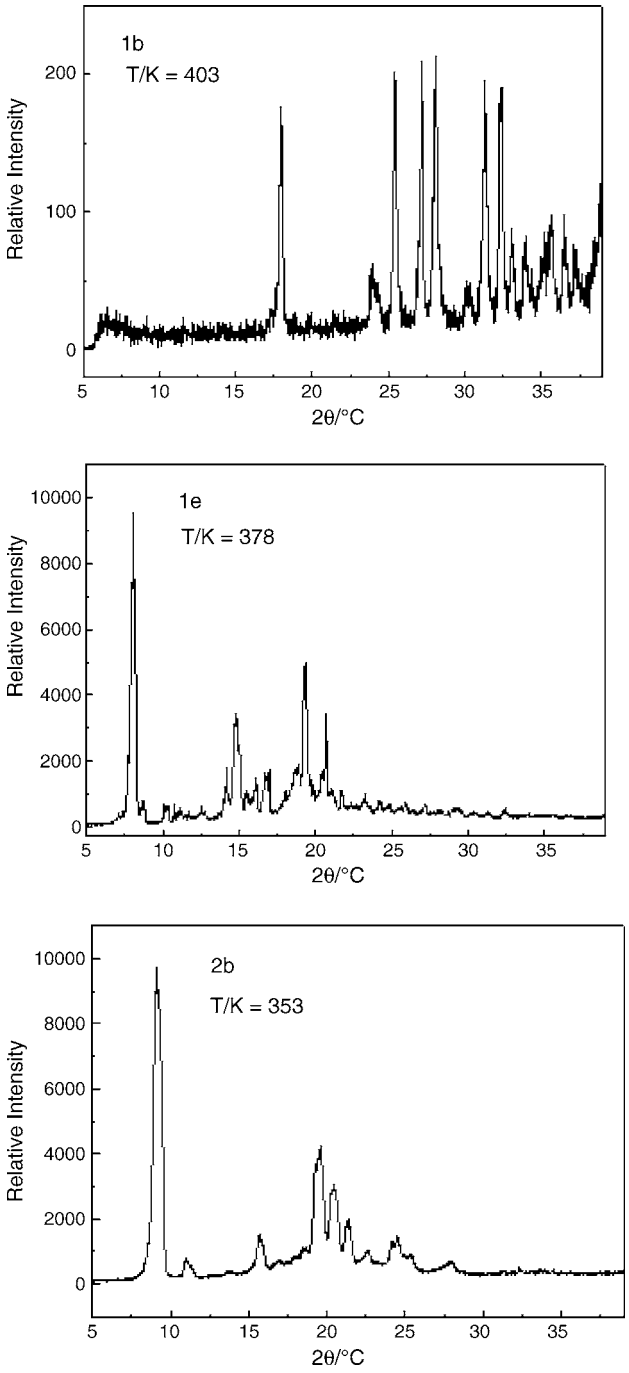

Fig. 6. Characteristic parts of X-ray diffraction patterns taken during the heating cycles at 403 K (**1b**), 378 K (**1e**) and 353 K (**2b**), respectively.

rigid nuclei with the possibility of molecular aggregation by hydrogen bonds [11,12,15,16] and short flexible hydrocarbon chains (groups **1** and **2**) or attached rigid and planar phenyl or benzyl groups (groups **3** and **4**, and benzyl esters of **1**–**4**). The use of shorter and non-linear lateral substituents tends to disrupt the potential lamellar packing and LC phase stability. The ester polar group promotes lamellar packing and generates smectic phases, however, only in case terminal chains are both sufficiently long and linear. For the materials **3a**–**c** and **4a**–**c**, one might expect them to have bent molecular shape, which is not conductive towards the LC molecular packing. The regions of low polarizability are tetrahedral, and the regions of the high one are planar. Any changes in these regions might affect the way the whole ensamble of the molecules pack. Certain alternating combinations do not pack together in the manner required for the LC phase generation, although the influence of polar end groups on mesomorphic behaviour of symmetric smectogens shows that the ester derivative are capable of producing liquid crystals in a pure state [34]. Layered segregation and mesomorphic properties would probably promote the presence of long aliphatic chains, perfluorinated alkyl segments [35], a polar terminal group attached directly to an aromatic core, or the polymerization [21,36].

4. Conclusion

For *N*,*N*′-carbonyl-bis-(L-valine and L-leucine acid) the esterification leads to the increased number of polymorphic transitions and decreased transition temperatures. Entropy changes referred to the methyl ester as the most organized and to the benzyl ester as the most disorganized phases. *N*,*N*′-Carbonyl-bis-(L-phenylglycine and L-phenylalanine acids) showed an increase of the first transition temperatures upon esterification. The methyl esters of phenyalanine derivatives exhibited the best ordering. The highest values of transition temperatures have been noticed for racemic methyl esters as the most disorganized phase. All investigated *N*,*N*′-carbonyl-bis-(L-amino acids) showed the temperature of isotropization identical to their temperature of decomposition. For *N*,*N*′-carbonyl-bis-(L-amino acid methyl esters) a drop of transition temperatures was noticed by introduction of methylene unit. The structures of atromatic methyl ester derivatives showed less order but their order improved upon an introduction of methylene unit. *N*,*N*′-Carbonyl-bis-(L-amino acid benzyl esters) showed more disorganized phases after an introduction of one CH_2 unit. Although some strucutral elements indicated the possibity of LC phase formation, no mesophases have been confirmed by the XRD at chosen temperatures.

Acknowledgments

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