

## Solvent-free self-assembly of small organic molecules into fibrillar microstructures

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Self-assembly is an efficient approach for the preparation of supramolecular structures with sizes ranging from nanometers to micrometers. Investigation of self-assembled fibres and fibrils is in the focus of very active research as these materials have potential applications in tissue engineering, template for inorganic nanofibres, electrooptical materials, etc. Here we report that recently synthesized L-valine and pyridine containing low-molecular compounds, self-assemble under solvent-free conditions into fibril structures in solid state. Heating of a dry powdered sample caused formation of rod-like particles. The initially formed nanofibres evolved to microscale needles upon further heating. The habitus of the fibres grown remains stable upon cooling. Results obtained represent an interesting alternative for the preparation of organic crystalline nanoobjects and microfibres in solvent-free conditions.

**Key words:** low-molecular gelators, supramolecular complexes, organic nano- and microfibres.

### INTRODUCTION

The interest in new designs for self-assembly approaches in producing microscopically small objects continuously increases in the last decades [1–3]. An attractive morphology of such nano- and micro-items is the fibrous one as many properties (mechanical, electrical, optical, transport, etc.) can be controlled along the fibre sizes. Conventional methods used up to now in the preparation of supramolecular nano- and micro fibres from small molecular organic compounds involve work in solution. Here, we are describing organic compounds that are capable of self-assembling into fibres with nano- and micro-dimensions in the absence of solvent. Some examples for solvent-free processes like chemical reactions [4, 5], synthesis of nano-capsules [6], etc. are presented in literature and although they are still limited in number, obviously it is more economic and pure approach, definitely preferred, when it is applicable. It is also in a good agreement with the principles of green chemistry.

Recently we reported [7] that compound **1** (Fig. 1), which belongs to the family of the so-called low-molecular gelators (LMWG), forms gels or other precipitates in organic solvents and in water. All the solids obtained from its solutions (xerogels, spherulites, etc.) were found to be constructed by thin fibres which X-ray powder diffraction (XRPD) data showed the crystalline structure called **1 $\alpha$** . We found that when heating a powdered solid material from

**1 $\alpha$**  above 225°C, a solid state polymorphic transition took place leading to a fiber-like polymorph **1 $\beta$** . Polymorph **1 $\beta$**  was obtained also after melting of the product and cooling down to room temperature. XRPD, differential scanning calorimetry (DSC), infrared spectroscopy (IRS) and circular dichroism spectroscopy (CD) measurements gave an evidence of the solid-solid transformation [7].

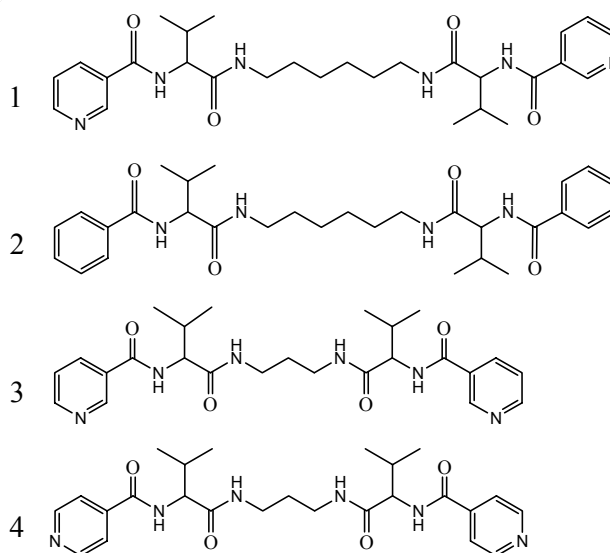


Fig. 1. Compounds used in the experiments.

Here we report that compounds related to **1** (Fig. 1) during the heating in the absence of solvents exchange their morphology and the particles, shapeless at the micro scale (Fig. 2a), self-organize into filament formations (Fig. 2b). The fibres formed belong to two types: the first one corresponds to

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straight fibres which are isolated and with no branching and the second one – to twisted pronged fibres that can even be wrapped as rope. Their habitus depends on the chemical structure and conditions of obtaining (Fig. 2, 3). Polymorphic exchange noticed for compound **1** during the heating [7] (Fig. 4.1) is not always observable with the other compounds. Noticeably, the fibres obtained from compounds **3** and **4** under the same conditions possess helical structure (Fig. 3a, b, d, e), which is a very good example for amplification of molecular chirality in supramolecular aggregates. One of the active research fields nowadays concerns translation of chirality from molecular level to micro- and macro scale. It was pointed by other authors summarising the results obtained over the past decade that the predicting of amplification of chirality is challenging but still impossible [8].

## EXPERIMENTAL

Compounds used in this work are presented in Fig. 1. They were synthesized according to previously described protocols for compound **1** [7], **2** [9], **3** and **4** [10]. All they belong to the group of LMWG and form gels or other solid precipitates in different solvents. In order to check their self-assembly ability in the absence of solvent, demonstrated from compound **1**, as well as correlated with this process phenomena, e.g. solid state phase transition, a series of experiments was realised.

*Thermal treatment and preparation of samples for scanning electron microscopy (SEM).* Thermal treatment of the substances was done in two ways. First one was similar to that explained for compound **1** [7]. Briefly: Sample of well-crushed material obtained as a product of the synthesis, or after recrystallization (xerogel, spherulites, etc.), was put on a cover glass slide, placed over a heating plate and observed with the loupe while heating. Along the heating, at temperatures individual for each compound, the powdered material (Fig. 2a) starts to rearrange into fibril objects. Keeping the temperature higher than this one and lower than the melting point leads to exchanges of the fibril sizes. Temperature intervals and time of heating are individual. The observed habitus remained stable upon cooling the samples to room temperature. A number of samples were prepared and for each one the heating was stopped at a different level of shape exchange, left for cooling and used for SEM studies (Fig. 2b, c, Fig. 3a, b, d, e). Second way for preparation of patterns for SEM studies was in DSC apparatus. We tried to relate conditions of the open system with those in a closed system in DSC pans,

where all parameters were strictly defined. In DSC pans, the powdered material was enclosed, sealed very well and thermal conditions were set before starting the experiments. After cooling, the pans were opened and transformations were recorded by SEM observations (Fig. 3c, f).

DSC measurements also were done to follow the thermal behaviour of the compounds, in order to have precise data for melting points and polymorphic transitions, in case they take place. XRPD, IR and CD measurements of solids obtained from solutions as well as after thermal treatment at specific temperature were performed in order to determine the characteristics of these materials and any relation between them.

## RESULTS AND DISCUSSION

First of all, we should notice again that all compounds from Fig. 1 belong to LMWG. Results, concerning the behaviour of these compounds in solutions, show that all they always make gels or solid precipitates, constructed from thin fibrils and their structure was studied by electron microscopy [7, 9, 10]. Xerogels and other solid precipitates that were formed in the supersaturated solutions of compound **1** showed no branched adhered each to other fibers with diameter about a micron [7]. The morphology of solids obtained from compound **2** solutions is similar to that found for compound **1** [9]. Detailed studies of xerogels from each of the four compounds revealed elongated objects of different size (in nano- and microscale) [9], as well as entangled network of fibres [10].

### *Thermally-induced self-assembly in the absence of solvent*

As it is mentioned above, during the heating of ground material the morphology of the powdered substance exchanges and compound reorders into fibrils. Depending on the substance and conditions of thermal treatment two main types of fibrils have been obtained. Compounds **1** and **2** (Fig. 4) have very close melting points (270 and 276°C), both reveal solid-state self-assembly in the same temperature range (~ 220–270°C) and the obtained crystalline needles look straight and very well shaped rods. Needles obtained from both compounds have similar morphology; nevertheless they have been prepared on the heating plate in the hood, or in DSC pans. Fig. 2 presents fibres obtained from **1** and **2**, the sizes and number of the needles for any of these two compounds depend on amount of the used material and thermal regime (temperature, time and rate of heating).

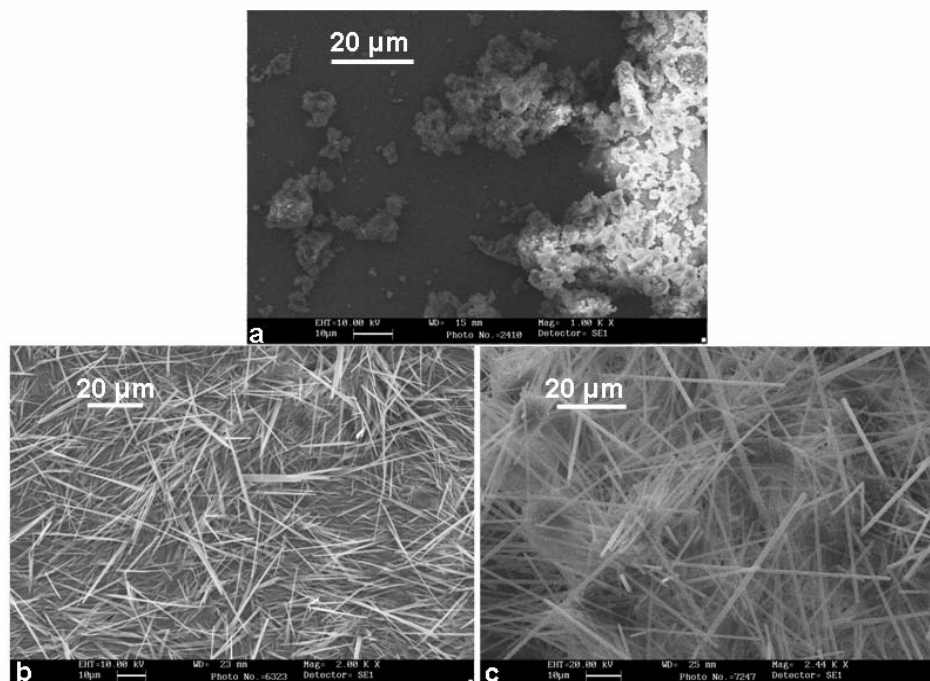


Fig. 2. Crystalline microfibrils obtained from **1** and **2**: a – Sample of the starting grounded material; b, c – Straight needles formed during the thermal treatment from **1** (b) and **2** (c).

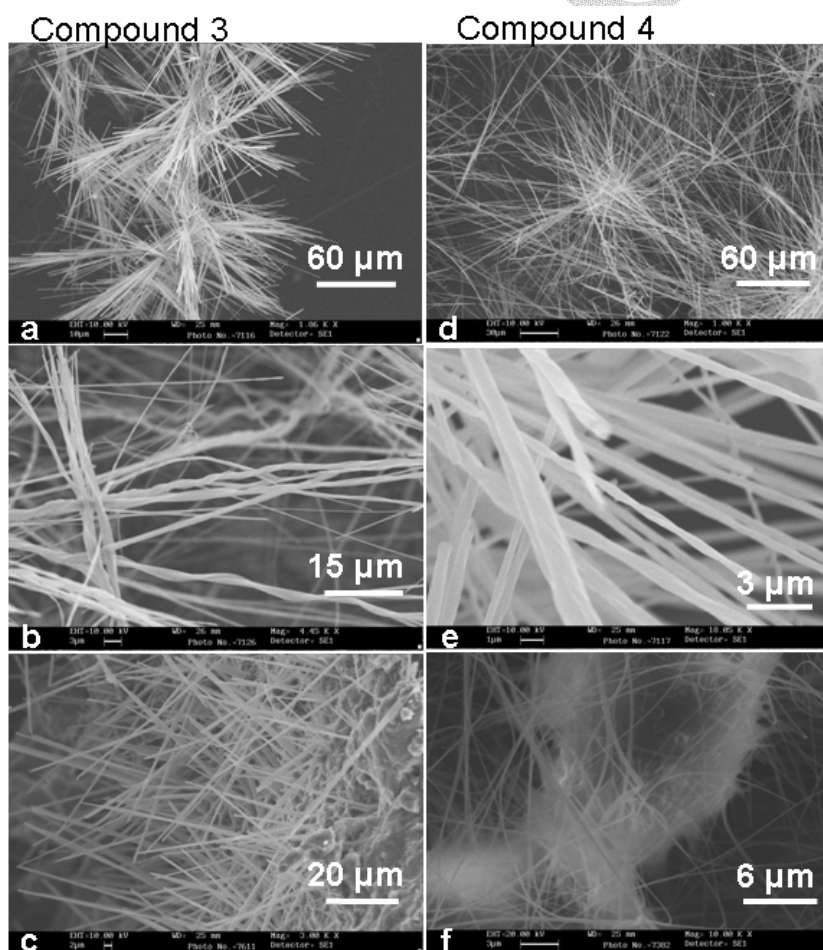


Fig. 3. Fibrils obtained from compounds **3** and **4** on the heating plate and in the DSC pans: a-c – Compound **3**; d-f – Compound **4**; a, b, d and e – Samples obtained on a heating plate; c and f – Samples obtained in the DSC pans.

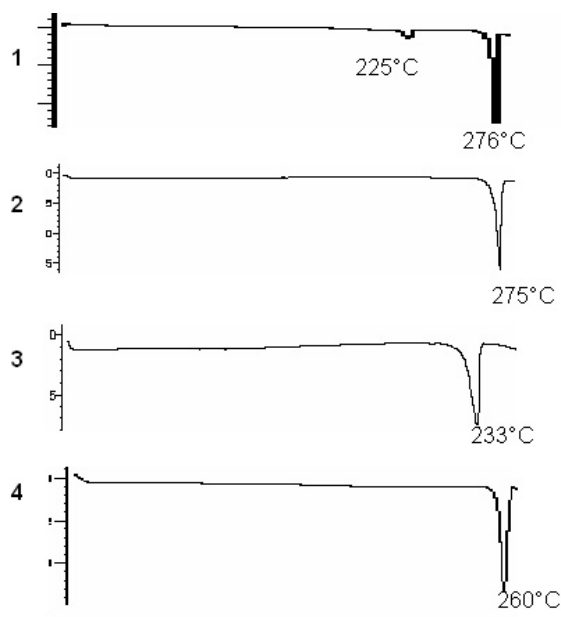


Fig. 4. DSC data for compounds **1**, **2**, **3** and **4**, prepared according to the protocols described in [7, 9, 10].

Compounds **3** and **4** also self-organize into fibril shapes. The type of the fibrils obtained for these two compounds depend on the conditions of thermal treatment, too. The most important difference for these two compounds in comparison with the first two, is the fact that they self-assemble into helicoidal structures in case of thermal treatment on the heating plate (in the hood) (Fig. 3a, b, d, e). When the heating was performed in DSC apparatus again straight fibres (at the highest possible magnifications) were observed (Figs. 3c and 3f).

#### *Thermally induced self-assembly in the presence of solvent*

As it was reported before, compound **1** in all solids obtained from different solvents has one and the same crystalline structure, denoted as **1 $\alpha$** , which structure during the heating undergoes polymorphic transition at  $\sim 225^\circ\text{C}$  to **1 $\beta$**  (Fig. 4). Then, at up of  $225^\circ\text{C}$  starts rearrangement of **1 $\beta$**  in the crystalline nano- and microfibres [7] (Fig. 2b). Compound **2** does not reveal such transition no matter how the solid was obtained (Fig. 4.2). Compounds **3** and **4** do not show such solid-solid transition in the forms obtained as products of synthetic reaction (Fig. 4.3 and 4.4). In some cases, depending on the solvent and conditions of preparations, **3** and **4** also undergo such transitions, but, obviously, it is not influential for the crystals shape exchanging. DSC studies show also that the exact place of peak(s) denoting

phase transitions depends on the solvent used for the solution prepared before gelation or precipitation.

The four compounds make gels, spherulites and other formations from supersaturated solute but single crystal was impossible to obtain from any of these compounds.

All solids formed from solutions or after thermal treatment are represented by very thin 1D formations (Figs. 2 and 3), which cannot be used for routine XRD analysis. That is why XRPD have been done only to the starting materials and those obtained after prolonged heating at temperatures, at which morphology transformation took place. XRPD spectra for the four compounds are represented in the Fig. 5 and its four subfigures (5.1–5.4). Two spectra for each compound are given – before and after thermal treatment. All XRPD spectra contain very sharp peaks, which means that all used samples are crystalline, but spectra, obtained after the heating, show low amount (not more than 10%) of amorphous phase. As it is seen from Fig. 5.1, only compound **1** has entirely different diffractograms, which testifies to two different polymorphic phases. Completely identical diffractograms were registered for compound **2**, no matter the spectra are taken before or after thermal treatment, which is in accordance with DSC data that this compound changes its morphology during the heating, but does not change its polymorphic state. Compound **3** has the same behaviour like compound **2**. In case of compound **4** (Fig. 5.4) all peaks characteristic for the thermally treated form (e.g.  $2\theta = 6, 9.8, 18.5$ ) were observed in the pattern of solution obtained solid. Probably, compound **4** crystallizes from the solution in a mixture of two or more polymorphs.

CD signals confirm that thermal treatment of compound **1** leads to rearrangement of the molecules into different mode, while for all other compounds any significant difference has not been noticed. In Fig. 6 the CD spectra of the compounds are presented and all they have negative absorbance at about 230–235 nm, which corresponds to the aromatic  $\pi$ - $\pi^*$  transition, and many of them have well-defined absorbance at about 280 nm, which, most probably, is associated with carbonyl/aromatic transitions.

IRS data for compounds **2**, **3** and **4** are also in accordance with the other results. The IR spectra [9, 10] are absolutely identical for both materials (before and after thermal treatment) and, because of that, they are not presented here.

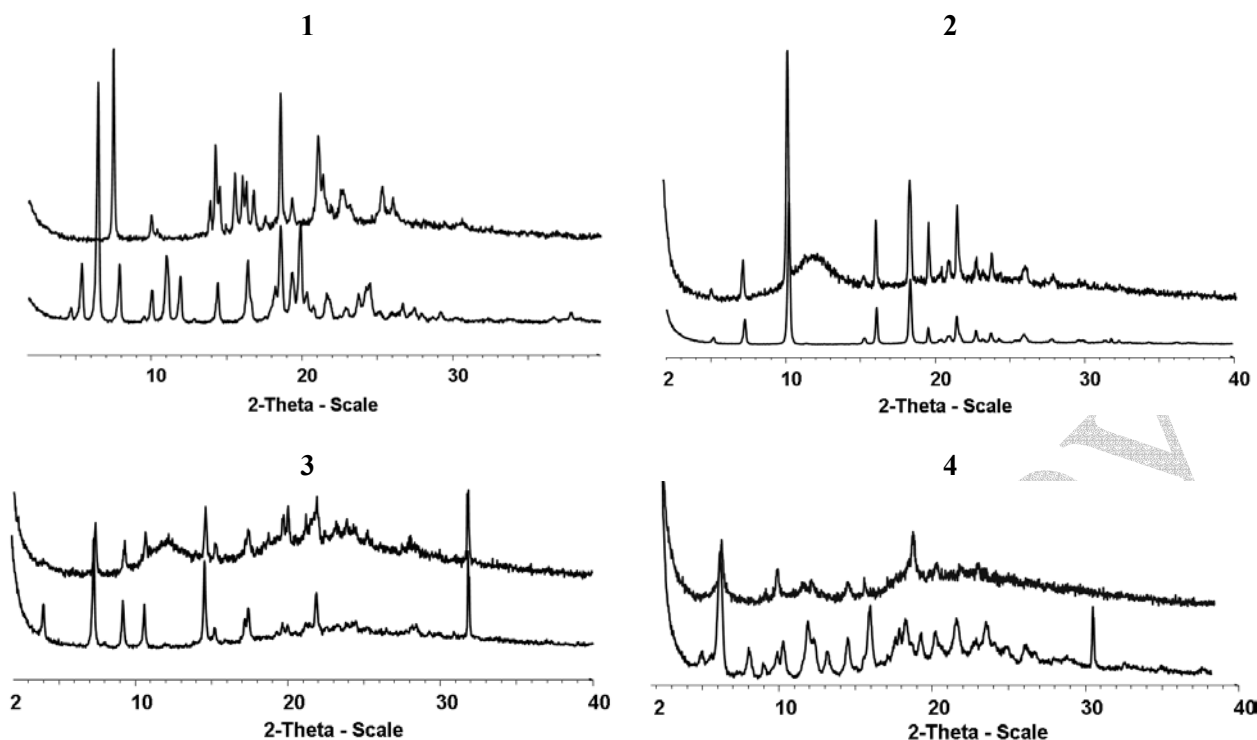


Fig. 5. XRPD spectra of the four compounds before (bottom line) and after (top line) thermal treatment.

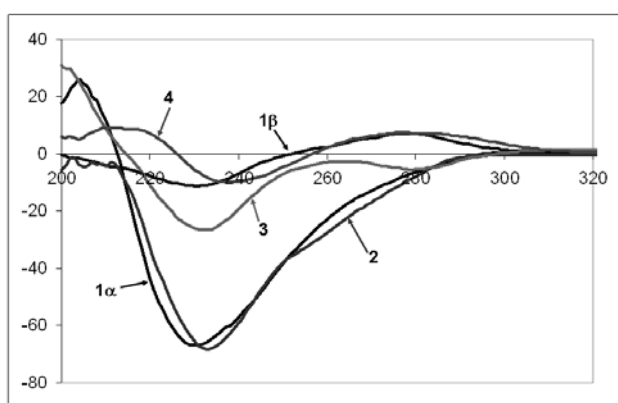


Fig. 6. CD spectra of compounds **1 $\alpha$** , **1 $\beta$** , **2**, **3** and **4** (KBr pellets 0.25% w/w).

On the basis of the results for solid-state polymorphic transition and solvent-free self-assembly of compound **1**, recently reported by us [7], we amplified this study on more compounds with similar structures and found that all they are capable of solvent-free self-assembly during heating. It turned out that the solid-state polymorphic transition is not a main condition for fibril formation, as for more compounds it does not take part. One of the possible reasons for the solid-state self-assembly observed in the described experiments is sublimation and deposition in new crystalline fibril formations

## CONCLUSIONS

As a conclusion, we present a new approach for nano- and microfibrils formation at solvent-free

conditions that can substitute commonly applied work in solution aiming fibre formation. All used compounds tend to form fibril networks in solutions and we have shown that this property is manifested without using solvents. This self-assembly procedures are advantageous from technical and environmental points of view and they are related to active research in solvent-free procedures for organic and organometallic synthesis [4, 5]. Fibrils, formed at some conditions, are an interesting example of amplification of molecule's chirality to supramolecular complexes that could be used in appropriate fields as asymmetric catalysis, molecular recognition, optoelectronics, etc.

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## САМОПОДРЕЖДАНЕ НА МАЛКИ ОРГАНИЧНИ МОЛЕКУЛИ В НИШКОВИДНИ МИКРОСТРУКТУРИ В ОТСЪСЪТВИЕ НА РАЗТВОРИТЕЛ

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(Резюме)

Самоорганизацията е един ефикасен подход за получаването на надмолекулни комплекси с размери от порядъка на нано- до микрометри. Изучаването на този процес в случай на образуване на нишки и влакнести структури е обект на активни научни изследвания, тъй като получените с такава морфология материали имат потенциално приложение в тъканното инженерство, като шаблони за неорганични нанонишки, материали в електрооптиката и др. Тук съобщаваме за наскоро синтезирани нискомолекулни производни на L-валина и пиридина, които се самоорганизируют в нишкови структури в твърда фаза, т.е. в отсъствие на какъвто и да е разтворител. Нагряването на сухото разпръснато вещество води до образуването на игловидни частички с наноразмери, които се развиват в микро-пръчици при продължаващо нагряване. Хабитусът на нарастнатите нишки се запазва и след охлаждане. Получените резултати представят интересна алтернатива за получаването на кристалинни органични нанообекти и микро-нишки в условие на отсъствие на разтворител.