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Hydrogelators

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Chapter 6

Benzene triamide amino acid hydrogelators

Abstract

The rational design of a new hydrogelators is a long standing aspiration in the field that has relied, with few exceptions, on trial and error as well as serendipity to date.^{1,2} The experience gained and understanding developed in previous studies based on the triamide-cyclohexane/amino acid combinations in previous chapters, should form the basis for a rational approach to designing new hydrogelators. In this chapter we show that a new hydrogelators can be obtained by combining key motifs used in two distinct classes of low molecular weight hydrogelators. We test the hypothesis: key structural motifs from benzenetriamides and cyclohexanetriamides can form the basis of a novel hydrogelator.

Introduction

The benzene triamide core (**BTA**, Figure 1), which is typically the basis for organogelators, has been used in hydrogelation also.³ In the latter case, supramolecular polymerization in water it requires large hydrophobic and hydrophilic tails to achieve gelation.⁴⁻⁶ While the cyclohexane triamide core (**CH**, Figure 1), used thus far in this thesis, can form gels with simple amino acid side groups.⁷⁻⁹ However, the cyclohexane core is less suitable for applications than the BTA core due to cost and the stereochemical demands it introduces.⁷ Furthermore, the BTA core is spectroscopically useful due to its moderate absorption in the UV region.

The supramolecular packing in the gel fibres in both classes differs slightly. The accepted model for packing in BTA gels is based on the crystal structure of **1** (Figure 1), which shows helical stacking of the core structure with hydrogen bonding of the amides at a 45° angle with respect to the core benzene.¹⁰ In contrast to this the packing of **CH** gels is based on the crystal structure of **CH-Tyr** (Figure 1), which show linear stacking of the cyclohexanes and hydrogen bonding of the amides at 90° with respect to the core.⁷ The helical twist in **BTA** that accompanies supramolecular assembly provides for an often strong CD signal that is a powerful probe in investigating the temperature dependence of stacking.³

In this chapter we show a compound based on the **BTA** core and the amino acid groups, used in **CH** gels, to engage in hydrogelation. We report two compounds that show promising gelation behaviour. The methionine based gelator with a cyclohexane core discussed in earlier chapters is the gelator with the lowest CGC and was therefore used as a starting point. Valine was chosen also as, although it does not form gels with the **CH** core, its analogue leucine does. The **BTA** core is expected to be more hydrophobic than, and present π - π interactions absent in, the cyclohexane core and hence an amino acid that is less hydrophobic than leucine will balance the effect on solubility and allow for gelation. The gels obtained were characterized by dropping ball, rheology, UV-Vis absorption, CD and polarized Raman spectroscopy.

Synthesis

Two variations on the **BTA** core with amino acid tails were synthesized, **BTA-Val** and **BTA-Met** (Figure 2), as white powders with a yield of ~25%. Detailed description of synthesis and spectroscopic data is available in Appendix B.

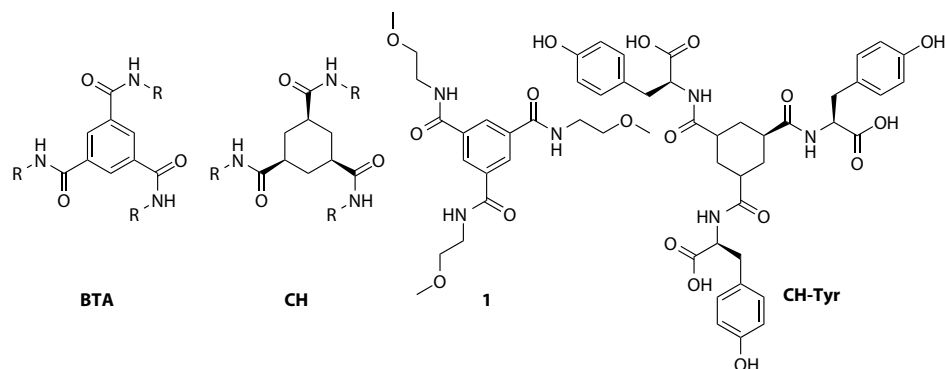


Figure 1. Structures of the **BTA** core, the **CH** core, **1** and **CH-Tyr**.

* At current specialty chemical prices (Sigma Aldrich) 1 g of **1,3,5-Cyclohexanetricarboxylic acid** is €115, while a 100 g of **Benzene-1,3,5-tricarboxylic acid** is €74.80.

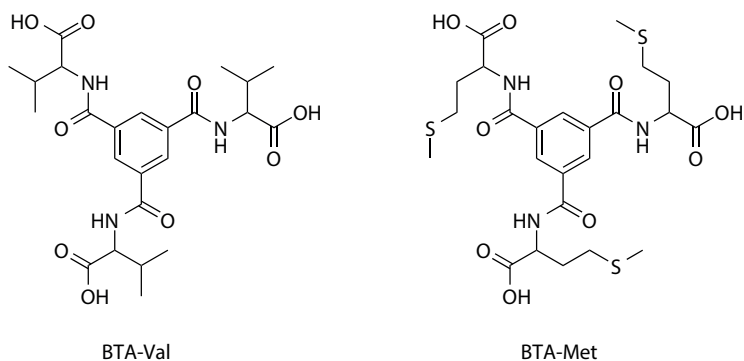


Figure 2. Structures of **BTA-Val** and **BTA-Met**.

Gel Properties

BTA-Val forms stable hydrogels at 5 mg/mL and **BTA-Met** forms hydrogels at 15 mg/mL however, the gels formed of **BTA-Met** deteriorate within 12 h. **BTA-Val** shows thermal stability up to 120 °C and has a G' of 1610 Pa and a G'' of 574 Pa, the formed gels showed no visible deterioration over a month. Both compounds do not form gels with pH switching from basic to acidic solutions but instead undergo precipitation. $^1\text{H-NMR}$ spectra of the compounds in basic or acidic water show that for Met 32% at 15 mg/mL stays in solution upon acidification and for Val only 8% at 5 mg/mL. The substantially lower solubility of **BTA-Val** compared to **BTA-Met** is likely key to gel formation, as for systems with a cyclohexane core 10% solubility is observed for gel forming compounds.^{chapter 3}

A band at 210 nm with a shoulder at 250 nm is observed in the UV-Vis absorption spectra of **BTA-Val** and **BTA-Met**. This absorption band does not show a CD signal over the range of 20 to 90 °C.

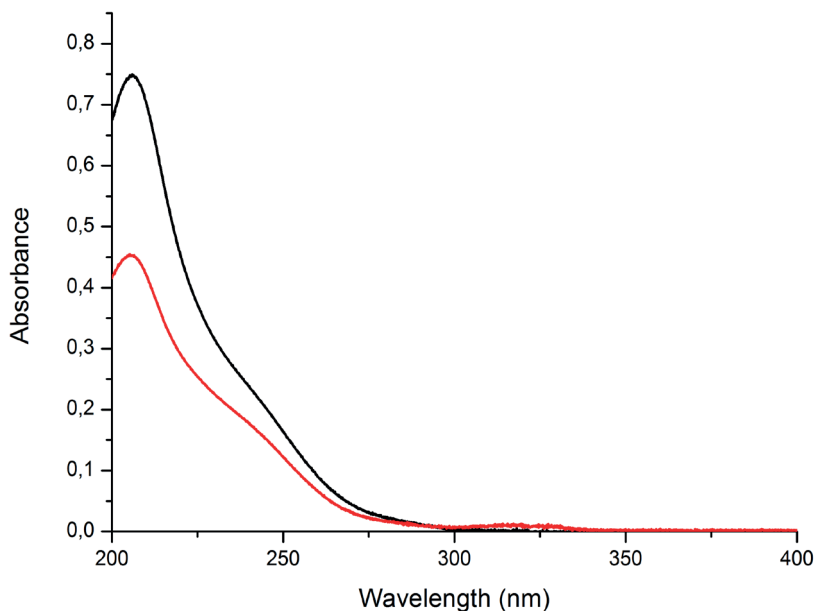


Figure 3. UV-Vis absorption spectra of **BTA-Met** (black) and **BTA-Val** (red).

Polarised Raman microspectroscopy

BTA-Val forms long fibrous structures, under a confocal microscope, which show a dependence of the Raman spectrum recorded at 785 nm on laser polarization. The band at 1004 cm^{-1} is due to deformation of the aromatic core of **BTA-Val** and shows a dependence on the direction of laser polarization with respect to fibre axis concomitant with that observed for the aromatic ring breathing mode at 1591 cm^{-1} . These data indicate that the aromatic rings are aligned as in the crystal of the model compound **1**.¹⁰ The band at 1620 cm^{-1} corresponds to the amide I vibration and has an angle

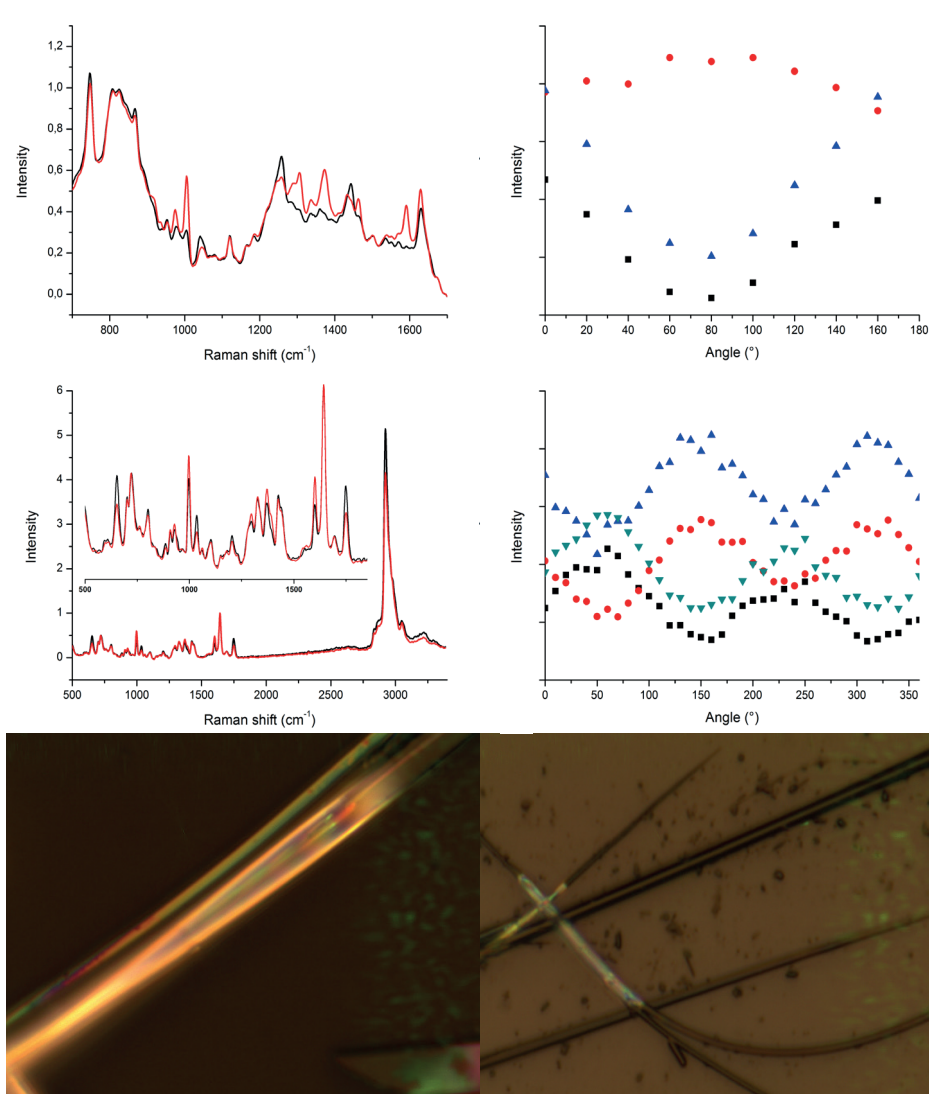


Figure 4. Top left: Raman spectrum **BTA-Val**. Top Right: Intensities of the bands at 1591 (black), 1257 (red) and 1004 cm^{-1} (blue). Middle left: Raman spectrum of **BTA-Met**. Middle right: intensity profiles of the bands at 1748 (black), 1600 (red), 996 (blue) and 652 cm^{-1} (green). Bottom left: microscope image (100x objective) of **BTA-Met**. bottom right: microscope image (100x objective) of **BTA-Val**.

of 45° to the aromatic core in the crystal structure and here we see that the oscillation of this band has the same period as the band at 1591 cm⁻¹.

BTA-Met forms long fibrous structures which show polarization dependence of the Raman spectrum recorded at 532 nm. The band at 996 cm⁻¹ is due to deformation of the aromatic core of **BTA-Met** and shows a dependence on polarization concomitant with that observed for the aromatic ring breathing mode at 1600 cm⁻¹. These data indicate that the aromatic rings are aligned as in the crystal of the model compound **1**.¹⁰ The band at 1748 cm⁻¹ could correspond to the amide I vibration and has an angle of 45° to the aromatic core in the crystal structure and here we see that the oscillation of this band is the opposite of the band at 1600 cm⁻¹.

Conclusion

We have shown that by combining the BTA core with three amino acid side groups from cyclohexane based gelators we can design compounds that form hydrogels. Both **BTA-Met** and **BTA-Val** form opaque hydrogels. The gels from **BTA-Met** are unstable and precipitate after 24 hours. **BTA-Val** forms stable gels for weeks. From the polarisation dependency of the Raman signals of the formed fibres it is shown that the aromatic core is aligned as in the crystal structure of **1**.

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