

## Fiber formation in water by a mono-urea dicarboxylic acid†

Lara A. Estroff, Jessica S. Huang and Andrew D. Hamilton\*

Department of Chemistry, Yale University, PO Box 208107, New Haven, CT 06520-8107, USA.

E-mail: andrew.hamilton@yale.edu; Fax: 203-432-3221; Tel: 203-432-5570

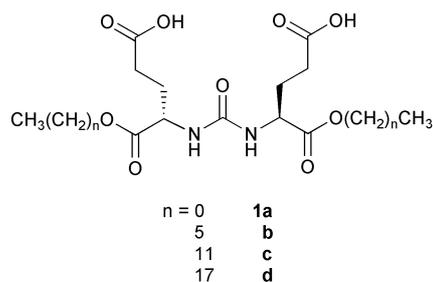
Received (in Columbia, MO, USA) 4th June 2003, Accepted 30th September 2003

First published as an Advance Article on the web 17th November 2003

Fibers formed by a mono-urea dicarboxylic acid derivative in water were analyzed by SEM, IR and XRD. The resulting data were used to develop a model of the molecular aggregation leading to fiber formation.

We have previously reported on the synthesis and effective gelation properties of a family of bis-urea dicarboxylic acid organic hydrogelators.<sup>1</sup> To understand better the structure–property relationships in these molecules we prepared a group of mono-urea dicarboxylic acids. The monoureas were not hydrogelators but formed fibers and ribbons of varying widths depending on the counterion used. Fiber formation in water by amphiphilic and bolaamphiphilic organic molecules is well documented and part of a continuum that includes hydrogels.<sup>2</sup> The goal of this present study was to better understand those factors in molecular design that favor gelation over precipitation of fibers.

The mono-urea, dicarboxylic acid derivatives, **1(a–d)**, were synthesized *via* the protected glutamate ester *p*-nitrophenol carbamate.<sup>3</sup> Monourea derivatives containing varying alkyl chains were prepared since gelation of water often results from a balance of hydrophobicity to hydrophilicity in a given molecule. In Tris buffer (50 mM, pH 7.6 and 8.8), **1c** (4 mM)‡ formed fibers depending on the pH and cation concentration and identity. However, none of the other derivatives (**1a,b,d**) showed any interesting aggregation behavior in aqueous solutions: they were either too soluble (**1a,b**) or precipitated as amorphous material (**1d**).



The fibers formed by **1c** were further investigated in order to develop a molecular model of the recognition events leading to aggregation. First, fiber formation by **1c** was investigated in the presence of mono-valent cations ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ ,  $\text{Cs}^+$ ,  $\text{NH}_4^+$ ) at both pH 7.6 and 8.8 (Tris buffer). At pH 7.6 fibers were formed with all mono-valent cations. At pH 8.8, only  $\text{Na}^+$  caused significant fiber formation. In the presence of  $\text{Rb}^+$  and  $\text{Cs}^+$  very small, delicate fibers could be observed with a polarizing light microscope at high magnification ( $\times 225$ ) while with  $\text{K}^+$  and  $\text{NH}_4^+$ , **1c** is soluble. Addition of di-valent cations ( $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Sr}^{2+}$ , and  $\text{Ba}^{2+}$ ) led to almost immediate precipitation of amorphous material suggesting that no fibers are observed due to a kinetic effect: the di-valent salts of **1c** are so insoluble that precipitation occurs before ordered structures can develop.

Light microscopy and SEM were used to investigate the morphology of the fibers formed with different cations (Fig. 1). From the SEM images, several observations stand out: 1) the fibers

formed with  $\text{NH}_4^+$  are significantly wider than the others, 2) the fibers formed with  $\text{Na}^+$  at both pH 7.6 and 8.8 are thinner and appear to be more flexible and 3) the fibers of **1c** with  $\text{K}^+$ ,  $\text{Rb}^+$ , and  $\text{Cs}^+$  have similar dimensions and morphologies. To determine if the relationship between morphology and cation corresponded to similar trends in aggregation patterns, IR spectroscopy and X-ray powder diffraction were employed.

IR spectroscopy can be used to identify the presence of hydrogen-bonding among urea groups and also to determine the protonation state of carboxylic acids.<sup>4,5</sup> For these reasons, IR was used to investigate the fibers formed by **1c** in the presence of different cations (Table 1 and supporting information). Interestingly, as was observed from the morphology of the fibers, the spectra of the  $\text{K}^+$ ,  $\text{Rb}^+$ , and  $\text{Cs}^+$  fibers are almost indistinguishable while those of  $\text{Na}^+$  and  $\text{NH}_4^+$  are noticeably different from each

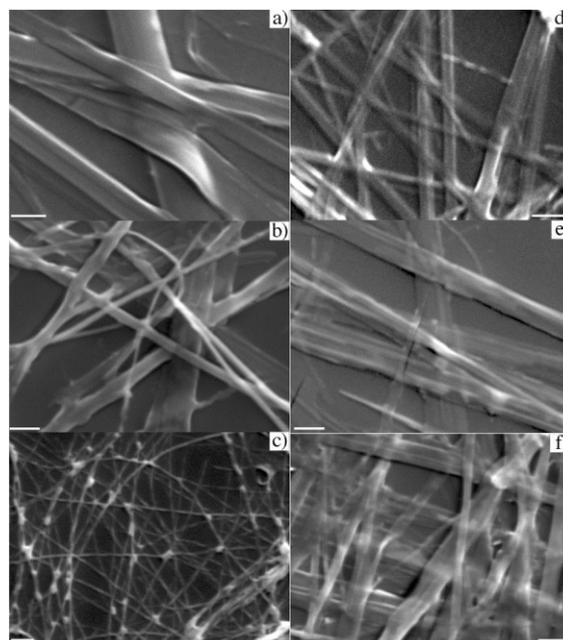


Fig. 1 SEM images of **1c** in the presence of a)  $\text{NH}_4^+$ , pH 7.6, b)  $\text{Na}^+$ , pH 8.8, c)  $\text{Na}^+$ , pH 7.6, d)  $\text{K}^+$ , pH 7.6, e)  $\text{Rb}^+$ , pH 7.6, and f)  $\text{Cs}^+$ , pH 7.6. Scale bars: 2  $\mu\text{m}$ .

Table 1 IR absorption bands (in  $\text{cm}^{-1}$ ) from the spectra of the fibers of **1c** formed in the presence of various cations in Tris buffer

Cation, pH	Ester/acid	Amide I	Amide II/ COO <sup>-</sup> asym
$\text{Na}^+$ , pH 8.8	1725	1638	1562 (br) <sup>a</sup>
$\text{Na}^+$ , pH 7.6	1733, 1718	1631	1561
$\text{NH}_4^+$ , pH 7.6	1726	1638	1571
$\text{K}^+$ , pH 7.6	1721	1630	1572
$\text{Rb}^+$ , pH 7.6	1722	1626	1572
$\text{Cs}^+$ , pH 7.6	1721	1625	1572
Organic	1721 (br) <sup>a</sup>	1641	1564

<sup>a</sup> br = broad.

† Electronic supplementary information (ESI) available: IR spectra and XRD patterns of **1c**. See <http://www.rsc.org/suppdata/cc/b3/b306351h/>

other. This suggests a common aggregation pattern for three of the cations. The shifts in the Amide I and II bands in the spectra of the  $K^+$ ,  $Rb^+$ , and  $Cs^+$  fibers of **1c**, as compared to the organic precipitate, are consistent with hydrogen-bonding of the ureas. The Amide I band shifts over  $10\text{ cm}^{-1}$  to lower wavenumbers ( $1641\text{ cm}^{-1}$  to  $1630\text{--}1625\text{ cm}^{-1}$ ) while the Amide II band shifts  $8\text{ cm}^{-1}$  higher ( $1564\text{ cm}^{-1}$  to  $1572\text{ cm}^{-1}$ ).<sup>6</sup> At pH 7.6, much above the  $pK_a$  of a normal carboxylic acid, **1c** appears to be only partially deprotonated based upon the sharpness of the Amide II peak and the spectral shape between  $1500$  and  $1400\text{ cm}^{-1}$  (see supporting information).<sup>6</sup> This suggests that the  $pK_a$  values of the carboxylic acids are modulated, presumably by the hydrophobic environment in the fibers, resulting in pH dependent behavior above the  $pK_a$  of a free carboxylic acid.<sup>4</sup> Only the spectrum of the fibers formed at pH 8.8 with sodium cations is consistent with a fully deprotonated carboxylate (broad bands at  $1562\text{ cm}^{-1}$  and  $1410\text{ cm}^{-1}$ ).

To obtain more information about the molecular scale organization in the fibers of **1c**, X-ray powder diffraction was used to evaluate the aggregates (Table 2 and supporting information).<sup>§</sup> The  $d$  spacing was found to vary (over  $7\text{ \AA}$ ) with cation suggesting that the cation is part of the long repeat (Table 2). However, there is neither a direct nor indirect relationship between the ionic radius of the cation and the long repeat distance if all of the aggregates are considered. Based on the microscopy and IR spectroscopy results, the  $Na^+$  and  $NH_4^+$  fibers appear to be formed *via* a different aggregation mode compared to the other cations. If  $Na^+$  and  $NH_4^+$  are excluded, there is an inverse relationship between ionic radius and  $d$  spacing for  $K^+$ ,  $Rb^+$  and  $Cs^+$  derivatives, further confirming a common motif for these aggregates. A  $5\text{ \AA}$  increase in  $d$  spacing is observed over a  $0.3\text{ \AA}$  decrease in ionic radius. Therefore, the change in radius is magnified ten-fold in the aggregate.

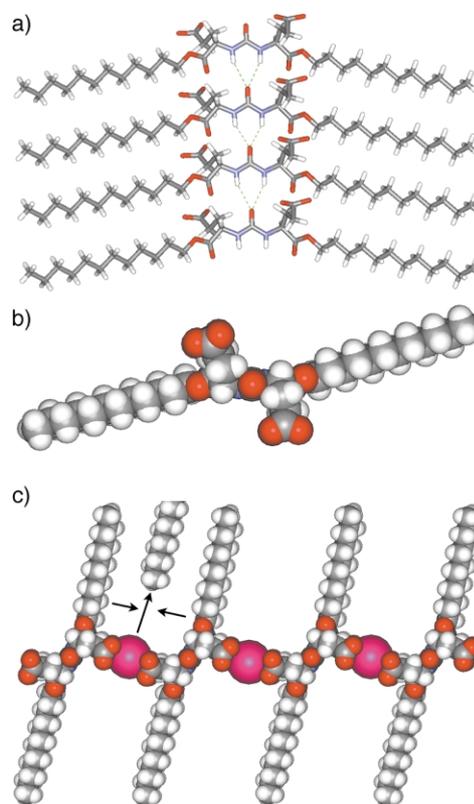
A possible model that accounts for this behavior is shown in Fig. 2. The mono-ureas can form one-dimensional hydrogen-bonded aggregates that project the carboxylates onto opposite sides of the ribbon (Fig. 2a,b). These 1-D fibers can then further aggregate *via* cross-linking of the carboxylates through binding to the cations (Fig. 2c). Further association of these hydrogen-bonded and metal-chelated networks can occur through interdigitation of the alkyl ester tails. As the diameter of the cation increases, the spacing between the two layers also increases, allowing further intercalation of the neighboring ribbons (arrows in Fig. 2c). In this way, the long repeat distance decreases as the diameter of the cation increases. The small size of  $Na^+$  and the acidity of  $NH_4^+$  may explain why these cations form ribbons *via* an alternate mode of aggregation. The ribbons formed by **1c** are too rigid (ordered) to form a gel and therefore precipitate from solution.

In summary, a new class of surfactants has been synthesized and one member, **1c**, has shown cation-dependent fiber formation in aqueous solution.

The authors thank the NSF (CHE0131477) for financial support of this research and Dr Jim Eckert, Geology Department, Yale University, for assistance with the XRD and SEM.

**Table 2** The long  $d$  spacings from the powder diffraction patterns of fibers of **1c** formed in the presence of various cations and the ionic radii of the cations

Cation, pH	Ionic radius/ $\text{\AA}$	Long $d$ spacing/ $\text{\AA}$
$NH_4^+$ , pH 7.6	1.50	40.8
$Na^+$ , pH 8.8	1.02	36.3
$Na^+$ , pH 7.6	1.02	36.4
$K^+$ , pH 7.6	1.38	39.2
$Rb^+$ , pH 7.6	1.49	36.5
$Cs^+$ , pH 7.6	1.70	34.0
Organic	—	37.8–38.1



**Fig. 2** A representation of a possible model of the aggregation of **1c** in the presence of  $Cs^+$  (pink) that leads to fiber formation. See text for details.

## Notes and references

‡ (*N*-L-glutamate dodecyl ester)carbonyl(*L*-glutamate dodecyl ester) (**1c**)  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.88 (t,  $J = 6.8\text{ Hz}$ , 6H), 1.26 (m, 36H), 1.65 (m, 4H), 1.99 (m, 2H), 2.20 (m, 2H), 2.42 (m, 4H), 4.16 (t,  $J = 6.7\text{ Hz}$ , 4H), 4.60 (m, 2H), 6.09 (m, 2H);  $^{13}C$  NMR (125 MHz) in  $CDCl_3$   $\delta$  14.1, 22.7, 25.8, 28.5, 29.3, 29.4, 29.5, 29.62, 29.65, 29.67, 30.4, 31.9, 52.5, 66.2, 173.6. HRMS (FAB) calcd for  $C_{35}H_{64}N_2O_9$  ( $M + 1$ )<sup>+</sup> 657.4690, found 657.4684. mp  $79\text{--}83\text{ }^\circ\text{C}$ .

§ The powder diffraction patterns were recorded on a Scintag PAD V X-ray diffractometer with a 2-theta goniometer and a liquid nitrogen cooled germanium semiconductor detector with  $CuK\alpha$  radiation with a nickel filter at 45 kV and 40 mA. The scans were taken at a step size of 0.02 degrees and a rate of 0.5 degrees/minute. The dried and powdered samples were mounted on glass slides using a small drop of acetone (or other volatile solvent) to help secure them.

- L. A. Estroff and A. D. Hamilton, *Angew. Chem., Int. Ed.*, 2000, **39**, 3447; L. A. Estroff, L. Leiserowitz, L. Addadi, S. Weiner and A. D. Hamilton, *Adv. Mater.*, 2003, **15**, 38; G. Wang and A. D. Hamilton, *Chem. Commun.*, 2003, 310.
- J. H. Fuhrhop and J. Koning, *Membranes and Molecular Assemblies: The Synergistic Approach*, ed. J. Stoddart, Royal Society of Chemistry, Cambridge, UK, 1994; J. H. Fuhrhop and W. Helfrich, *Chem. Rev.*, 1993, **93**, 1565.
- N. Choy, K. Moon, C. Park, Y. Son, W. Jung, G. Choi, C. Lee, C. Kim, S. Kim and H. Yoon, *Org. Prep. Proced. Int.*, 1996, **28**, 173.
- M. Kogiso, S. Ohnishi, K. Yase, M. Masuda and T. Shimizu, *Langmuir*, 1998, **14**, 4978.
- M. Kogiso, T. Hanada, K. Yase and T. Shimizu, *Chem. Commun.*, 1998, 1791; T. Imae, Y. Takahashi and H. Muramatsu, *J. Am. Chem. Soc.*, 1992, **114**, 3414.
- R. M. Silverstein, G. C. Bassler and T. C. Morrill, *Spectrometric Identification of Organic Compounds*, John Wiley & Sons, Inc., New York, NY, 1991.