Soluble supramolecular polymers based on urea compounds

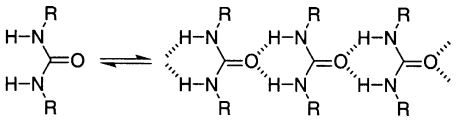
Sylvie Boileau, Laurent Bouteiller,*† Françoise Lauprêtre and Frédéric Lortie

Laboratoire de Recherche sur les Polymères (UMR C7581), CNRS, 2 rue Henri Dunant, BP 28, 94320 Thiais, France

Received (in Strasbourg, France) 1st August 2000, Accepted 22nd September 2000
First published as an Advance Article on the web 24th October 2000

N,N′-Dialkylureas, which form intermolecular hydrogen bonds, are interesting precursors in the field of supramolecular chemistry. Particularly, N,N′-di(2-ethylhexyl)urea, which is soluble in nonpolar solvents, was shown by viscosimetry and FTIR spectroscopy to be associated in heptane at concentrations higher than 10 g l^{-1}. The interactions involved are strongly reinforced by the cooperative association of two urea groups in the case of bis-ureas prepared from 2,4-toluene diisocyanate.

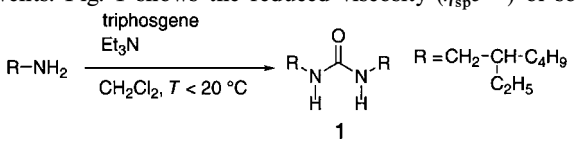
The design of self-assembling supramolecular polymers, which can be defined as arrays of small molecules held together by non-covalent interactions, is currently attracting considerable attention.[1–3] In the case of hydrogen-bonded supramolecular polymers that self-assemble in solution, most systems are based on A–A-type monomers[4–6] or A–A + B–B-type monomers.[7–9] Very few systems are based on A–B-type monomers[10–12] and, in most cases, association constants are weak. *N,N′*-Dialkyl or *N,N′*-diarylureas are A–B-type monomers that are known to self-assemble both in bulk[13–15] and in solution[12] in such a way that the two hydrogen atoms bound to a nitrogen atom are hydrogen bonded to the same C=O oxygen atom (Scheme 1). This prompted us to investigate new self-assembling A–B-type monomers based on the urea function.



Scheme 1

The simplest ureas, *N,N′*-dimethylurea and *N,N′*-diethylurea, are known to self-associate in nonpolar solvents such as benzene and carbon tetrachloride,[12] but their usefulness is limited by their low solubility in these solvents. Increasing the length of the alkyl groups to n-octyl or n-octadecyl does not significantly improve the solubility of dialkylureas, so we considered branched alkyl groups because branching is known to increase solubility. Of course, branching also increases steric hindrance, which could prevent urea functions from associating. Consequently, we selected a branched but not too bulky urea, *N,N′*-di(2-ethylhexyl)urea (**1**), which was synthesized from 2-ethylhexylamine and triphosgene (Scheme 2).

Dialkylurea **1** is indeed highly soluble in many nonpolar solvents. Fig. 1 shows the reduced viscosity ($\eta_{sp}c^{-1}$) of solutions of dialkylurea **1** in heptane, carbon tetrachloride and dichloromethane *vs.* concentration *c*. In dichloromethane, the viscosity is low and does not increase much with concentration, whereas it increases dramatically with concentration in heptane: for instance, at 40 g l^{-1} the viscosity of **1** in heptane is 40 times larger than in dichloromethane. The behavior in carbon tetrachloride is intermediate between the behavior observed in the other two solvents. Results obtained in these three solvents indicate that the lower the polarity of the solvent, the higher the viscosity, which is entirely consistent with the presence of an equilibrium between free and hydrogen-bonded dialkylurea **1** (Scheme 1): the lower the solvent polarity, the higher the association constant and therefore the longer the supramolecular polymer.



Scheme 2

The influence of concentration on association is shown by infrared spectra of **1** in carbon tetrachloride at three different concentrations [Fig. 2(a)]. In the part of the IR region shown, two bands can be seen, which belong to the free N–H resonance (3450 cm^{-1}) and the hydrogen-bonded N–H resonance (3360 cm^{-1}). At 6 g l^{-1} (0.02 M) dialkylurea **1** is highly associated, whereas at 0.1 g l^{-1} (4×10^{-4} M) it is mainly dissociated. Therefore, increasing the concentration of solutions of **1** shifts the equilibrium in favor of longer supramolecular polymers. Thus, dialkylurea **1** can be considered an A–B-type monomer whose association in nonpolar solvents leads to large supramolecular polymers.

In order to increase the magnitude of the association, bis-urea **2** (Scheme 3) was synthesized, because it has been shown that simultaneous formation of four hydrogen bonds can lead to very high association constants.[5] Moreover, bis-urea compounds have been recently reported to be efficient gelators for organic solvents[16–18] and to direct the association of peptide nanotubes in the solid state.[19] Unlike many related systems, which form a gel at room temperature after cooling of a hot

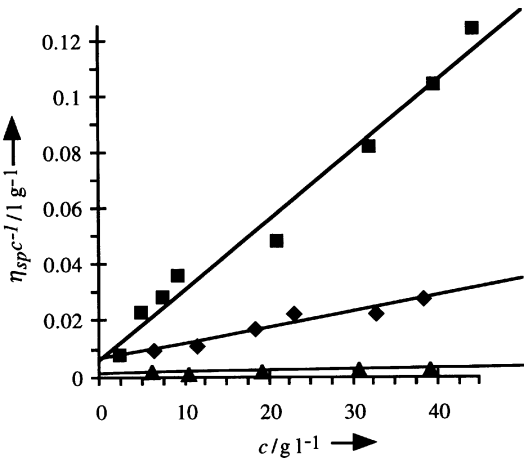


Fig. 1 Reduced (specific) viscosity in heptane (■), carbon tetrachloride (◆) and dichloromethane (▲) measured at 25 °C, *vs.* concentration *c* of dialkylurea **1**.

† *Present address*: Laboratoire de Chimie des Polymères, (CNRS UMR 7610), Université Pierre et Marie Curie, 4 place Jussieu, 75252 Paris cedex 05, France. E-mail: bouteiller@glvt-cnrs.fr

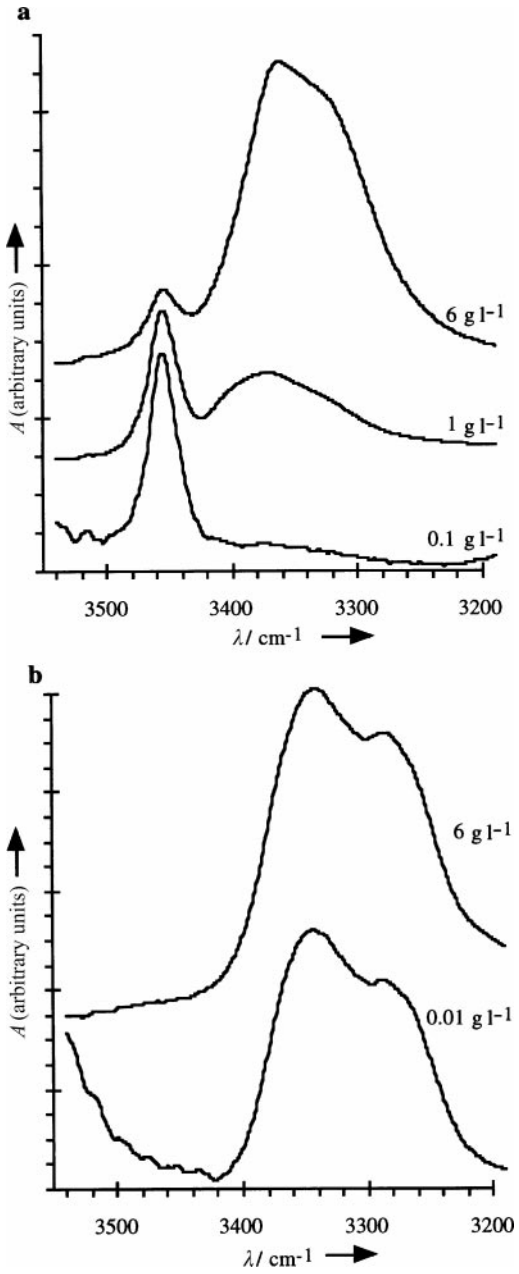


Fig. 2 FTIR spectra of solutions of different concentrations of (a) dialkylurea **1** and (b) bis-urea **2** in carbon tetrachloride at room temperature.

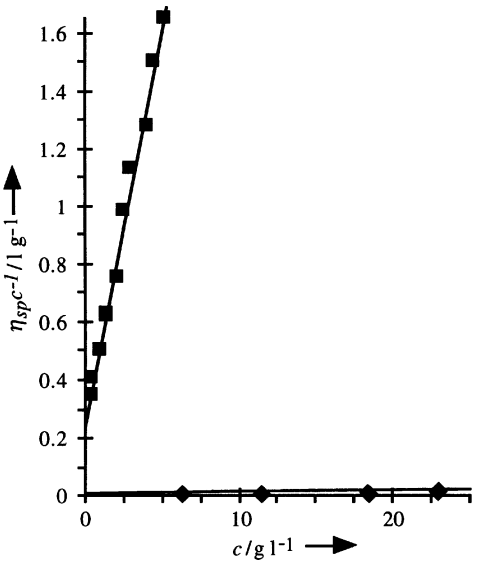
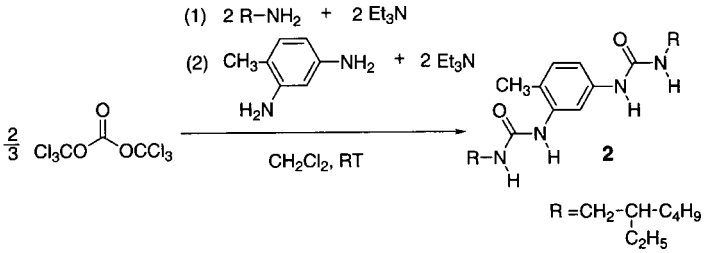


Fig. 3 Reduced (specific) viscosity of dialkylurea **1** (◆) and bis-urea **2** (■) in carbon tetrachloride measured at 25 °C, *vs.* concentration *c*.

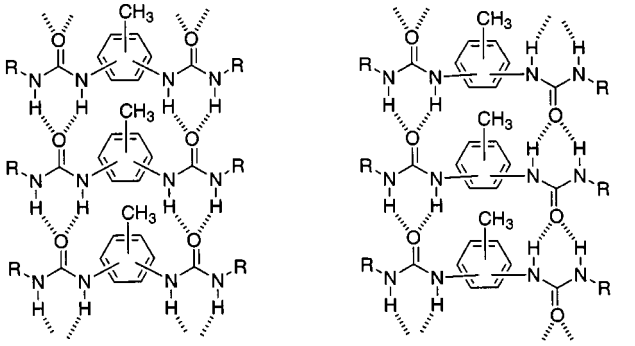
solution,[16–18,20,21] bis-urea **2** dissolves in carbon tetrachloride and heptane without heating. Moreover, dissolution is preceded by a swelling step as in the case of polymers.

Fig. 3 shows that the reduced viscosity of bis-urea **2** in carbon tetrachloride is extremely high and increases strongly with concentration. This high viscosity can only be due to the formation of high molecular weight species, which could be the consequence of two different types of association. First, the two urea functions borne by one molecule can be hydrogen-bonded independently to two different molecules: in this case, a highly branched and reversibly crosslinked structure is created, which explains the high viscosity. Moreover, these two urea functions can also hydrogen bond cooperatively[22] to the two urea functions borne by another molecule: in this case, a linear and very long structure is created, which also explains the high viscosity. In the first case, the fraction of free N–H groups of the two independent urea functions of bis-urea **2** should be of the same order of magnitude as the fraction of free N–H groups of dialkylurea **1**, whereas in the second case, the fraction of free N–H groups of the two cooperative urea functions of bis-urea **2** should be orders of magnitude lower than the fraction of free N–H groups of dialkylurea **1**. Fig. 2(b) shows that FTIR measurements support the second interpretation. Indeed, for concentrations as low as 0.01 g l^{-1} (5×10^{-5} M of urea functions), bis-urea **2** is fully hydrogen-bonded in carbon tetrachloride: no free N–H vibration can be detected. So in the same solvent and at the same temperature, dialkylurea **1** is totally dissociated at a concentration of 4×10^{-4} M, whereas bis-urea **2** is totally associated even at a concentration one order of magnitude lower. This result indicates that the association constant‡ for **2** is orders of magnitude larger than for **1**, and that hydrogen bonding of the two urea functions of **2** must be cooperative.

Different cooperative association patterns can be imagined. Two of them, which are consistent with molecular modelling studies and which have been proposed in the case of related systems,[16b,18,23] are represented in Scheme 4. In pattern **2a**, bis-urea **2** is associated in a polar fashion (parallel urea groups) and thus behaves as an A–B-type monomer. Due to conformational flexibility, bis-urea **2** could also associate according to pattern **2b**, in a nonpolar fashion (antiparallel urea groups) and thus it could behave as an A–A-type monomer. Of course, a higher level of organization is also possible: bundles of chains instead of single chains may be



Scheme 3



Scheme 4

formed. Studies are currently under way to determine the association pattern of bis-urea **2**.

In conclusion, we have shown that by choosing adequate substituents, it is possible to increase the solubility of urea compounds in nonpolar solvents. These compounds constitute a whole family of A–B-type monomers, which self-assemble to form supramolecular polymers. They open a new route to the self-assembly of star-shaped or branched supramolecular polymers. Strengthening the involved interactions is possible through cooperative association of two urea groups in a bis-urea such as **2**, which remains highly soluble in nonpolar solvents.

Experimental

2-Ethylhexylamine (Aldrich), triethylamine (Merck), triphosgene (Aldrich) and 2,4-toluenediamine (Aldrich) were used as received. Dichloromethane (SDS) was distilled over phosphorus pentoxide.

Syntheses

***N,N′*-Di(2-ethylhexyl)urea (1). 1** was prepared according to a procedure described previously[24] and slightly modified. To a stirred solution of 2-ethylhexylamine (10 g, 77 mmol) and triethylamine (11.5 ml, 83 mmol) in 125 ml of dichloromethane in an ice-cooled flask, triphosgene (4.1 g, 14 mmol) in 75 ml of dichloromethane was slowly added under nitrogen. The ice bath was removed and the mixture was stirred for 2 h before 100 ml of aqueous HCl (0.1 N) was added. The organic phase was separated, then washed with water until its pH was neutral, dried over magnesium sulfate and concentrated, leading to a crude oil. Purification was performed by dissolution in 100 ml of boiling acetonitrile and cooling to room temperature: a colorless viscous oil was recovered. After drying, 8.6 g (78% yield) of the expected product, the purity of which was checked by TLC, were obtained. Whatever the thermal treatment, no melting point was detected by DSC, only a T_g was observed at $-98\,^{\circ}C$. ^1H NMR (200 MHz, $CDCl_3$): δ 5.2 (s, 2H, NH), 3.0 (t, 4H, NCH_2), 1.2 (m, 18H, CH/CH_2), 0.8 (t, 12H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$): δ 159.0 (C=O), 43.0 (NCH_2), 39.6 (*C*H), 30.7/28.7/23.8/22.8 (CH_2), 13.8/10.6 (CH_3). Anal. calc. for $C_{17}H_{36}N_2O$: C, 71.77; H, 12.75; N, 9.85; O, 5.62. Found: C, 71.48; H, 12.78; N, 9.84; O, 5.66%.

2-Ethylhexyl-3-[3-(3-(2-ethylhexyl)ureido)-4-methylphenyl]urea (2). 2 was prepared according to a procedure described previously[25] and slightly modified. To a stirred solution of triphosgene (5.3 g, 18 mmol) in 100 ml of dichloromethane was slowly added a mixture of 2-ethylhexylamine (6.45 g, 50 mmol) and triethylamine (7.7 ml, 55 mmol) in 175 ml of dichloromethane under nitrogen with an HPLC pump, over a period of 28 h. Then, a solution of 2,4-toluenediamine (3.05 g, 25 mmol) and triethylamine (7.7 ml, 55 mmol) in 100 ml of dichloromethane was added in two portions. The mixture was stirred overnight and washed with 250 ml of aqueous HCl (0.1 N), 250 ml of aqueous KOH (0.1 N) and water until its pH was neutral. The organic phase was dried over magnesium sulfate, concentrated and purified by silica gel column chromatography with tetrahydrofuran–chloroform (15 : 85 v/v) as eluent. A first recrystallization in acetonitrile and a second one in ethyl acetate afforded 1.4 g of a white solid (13% yield), the purity of which was checked by TLC. Mp 185 °C (decomposition after melting). ^1H NMR (300 MHz, [D_6]DMSO): δ 8.3/7.5 (s, 2H, ArN*H*), 7.8 (s, 1H, Ar*H*), 7.1/6.9 (d, 2H, Ar*H*), 6.5/5.9 (t, 2H, CH_2NH), 3.0 (m, 4H, NCH_2), 2.1 (s, 3H, $ArCH_3$), 1.3 (m, 18H, CH/CH_2), 0.9 (t, 12H, CH_3). ^{13}C NMR (75 MHz, [D_6]DMSO): δ 155.4/155.3 (C=O), 138.7/138.3/129.9/118.6/111.1/109.5 (Ar), 41.5 (NCH_2), 30.5 (*C*H), 28.5/23.7/22.5/17.2 (CH_2), 14.0/10.6 (CH_3). Anal. calc. for $C_{25}H_{44}N_4O_2$: C, 69.40; H, 10.25; N, 12.95; O, 7.40. Found: C, 68.92; H, 10.30; N, 12.94; O, 7.71.

Methods

Infrared spectra were recorded at room temperature on a Perkin Elmer FTIR 1760 spectrometer in KBr cells of 0.05 to 5 cm path lengths. Carbon tetrachloride (SDS) was used as received.

Capillary viscosimetry was performed at $25 \pm 0.1\,^{\circ}C$ with a Cannon–Manning semi-micro viscometer. Solutions in heptane (SDS), carbon tetrachloride (SDS) or dichloromethane (SDS) were prepared one day prior to the measurements and filtered on Millex membranes ($\Phi = 0.45$ μm). The solvents were used as received.

Notes and references

‡ Attempts to measure an association constant for **2** in carbon tetrachloride failed because we were unable to obtain appreciable dissociation.

1 J. M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 1304.
2 C. M. Paleos and D. Tsiourvas, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1696.
3 N. Zimmerman, J. S. Moore and S. C. Zimmerman, *Chem. Ind.*, 1998, 604.
4 U. Keller, K. Müllen, S. De Feyter and F. C. De Schryver, *Adv. Mater.*, 1996, **8**, 490.
5 (*a*) R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe and E. W. Meijer, *Science*, 1997, **278**, 1601; (*b*) J. H. K. K. Hirschberg, F. H. Beijer, H. A. van Aert, P. C. M. M. Magusin, R. P. Sijbesma and E. W. Meijer, *Macromolecules*, 1999, **32**, 2696.
6 (*a*) S. Abed, S. Boileau, L. Bouteiller and N. Lacoudre, *Polym. Bull.*, 1997, **39**, 317; (*b*) S. Abed, S. Boileau and L. Bouteiller, *Macromolecules*, in press.
7 (*a*) C. Fouquey, J. M. Lehn and A. M. Levelut, *Adv. Mater.*, 1990, **2**, 254; (*b*) N. Kimizuka, S. Fujikawa, H. Kuwahara, T. Kunitake, A. Marsh and J. M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1995, 2103.
8 I. S. Choi, X. Li, E. E. Simanek, R. Akaba and G. M. Whitesides, *Chem. Mater.*, 1999, **11**, 684.
9 F. Würthner, C. Thalacker and A. Sautter, *Adv. Mater.*, 1999, **11**, 754.
10 P. Beak, J. B. Covington, S. G. Smith, J. M. White and J. M. Zeigler, *J. Org. Chem.*, 1980, **45**, 1354.
11 M. C. Etter, J. C. MacDonald and R. A. Wanke, *J. Phys. Org. Chem.*, 1992, **5**, 191.
12 J. Jadzyn, M. Stockhausen and B. Zywucki, *J. Phys. Chem.*, 1987, **91**, 754.
13 X. Zhao, Y.-L. Chang, F. W. Fowler and J. W. Lauher, *J. Am. Chem. Soc.*, 1990, **112**, 6627.
14 M. C. Etter, Z. Urbanczyk–Lipkowska, M. Zia–Ebrahimi and T. W. Panunto, *J. Am. Chem. Soc.*, 1990, **112**, 8415.
15 J. Perez–Folch, J. A. Subirana and J. Aymami, *J. Chem. Crystallogr.*, 1997, **27**, 367.
16 (*a*) J. van Esch, R. M. Kellogg and B. L. Feringa, *Tetrahedron Lett.*, 1997, **38**, 281; (*b*) J. van Esch, F. Schoonbeek, M. de Loos, H. Koojman, A. L. Spek, R. M. Kellogg and B. L. Feringa, *Chem. Eur. J.*, 1999, **5**, 937; (*c*) F. S. Schoonbeek, J. H. van Esch, B.

Wegewijs, D. B. A. Rep, M. P. de Haas, T. M. Klapwijk, R. M. Kellogg and B. L. Feringa, *Angew. Chem., Int. Ed.*, 1999, **38**, 1393; (*d*) F. S. Schoonbeek, J. H. van Esch, R. Hulst, R. M. Kellogg and B. L. Feringa, *Chem. Eur. J.*, 2000, **6**, 2633.
17 K. Hanabusa, K. Shimura, K. Hirose, M. Kimura and H. Shirai, *Chem. Lett.*, 1996, 885.
18 A. J. Carr, R. Melendez, S. J. Geib and A. D. Hamilton, *Tetrahedron Lett.*, 1998, **39**, 7447.
19 D. Ranganathan, C. Lakshmi and I. L. Karle, *J. Am. Chem. Soc.*, 1999, **121**, 6103.
20 Y. Yasuda, E. Iishi, H. Inada and Y. Shirota, *Chem. Lett.*, 1996, 575.
21 K. Hanabusa, C. Koto, M. Kimura, H. Shirai and A. Kakehi, *Chem. Lett.*, 1997, 429.
22 E. Di Cera, *Chem. Rev.*, 1998, **98**, 1563.
23 J. Malthête, A. M. Levelut and L. Liébert, *Adv. Mater.*, 1992, **4**, 37.
24 D. B. Grotjahn and C. Joubran, *Tetrahedron: Asymmetry*, 1995, **6**, 745.
25 P. Majer and R. S. Randad, *J. Org. Chem.*, 1994, **59**, 1937.