

11-Aminoundecanoic acid: a versatile unit for the generation of low molecular weight gelators for water and organic solvents

Anthony D'Aléo,^a Jean-Luc Pozzo,^a Frédéric Fages^{†,*a} Marc Schmutz,^b Gudrun Mieden-Gundert,^c Fritz Vögtle,^{*c} Vesna Caplar^d and Mladen Zinic^{*d}

^a LCOO UMR 5802, Université Bordeaux I, 33405 Talence Cedex, France

^b Institut Charles Sadron, CNRS, 6 rue Boussingault, 67083 Strasbourg Cedex, France

^c Kekulé-Institut für Organische Chemie und Biochemie, Gerhard-Domagk-Strasse 1, 53121 Bonn, Germany. E-mail: voegtle@uni-bonn.de

^d Laboratory of Supramolecular and Nucleoside Chemistry, Department of Chemistry and Biochemistry, Rudjer Boskovic Institute, 10000 Zagreb, Croatia. E-mail: zinic@rudjer.irb.hr

Received (in Columbia, MO, USA) 9th July 2003, Accepted 9th October 2003

First published as an Advance Article on the web 18th November 2003

The use of 11-aminoundecanoic acid as a synthetic building-block allows the systematic preparation of (oligo)amide organogelators—including chiral ones—which display remarkable gelation properties in organic solvents and water.

Low molecular weight organogelators have emerged recently as a fascinating new class of molecular systems that offer unique access to self-assembling thermoreversible materials displaying tailored properties.¹ Amide or urea derivatives based on α -amino acids represent a key family of gelator molecules. Indeed numerous systems have been reported to harden organic solvents² or water,³ or even to display ambidextrous behaviour.⁴ Recently we have shown that simple urethane, amide or urea derivatives of 11-aminoundecanoic acid (AUDA) are efficient gelators of polar organic solvents when i) the carboxylic acid function is deprotonated, and ii) the *N*-acyl substituent contains an aromatic terminal moiety.⁵ In line with these investigations, we decided to further investigate the potential of linear 1, ω -amino acids as alternatives to conventional

peptides for the systematic and easy generation of low molecular weight organogelators.⁶ A decisive clue to this is given by the fact that oligoamides related to nylons are well known to self-assemble into hydrogen-bonded sheets and to produce crystalline fibres.⁷ With this in mind, we have synthesized dodecanoylamines of 11-aminoundecanoic-acid-containing systems as representative examples of a new series of efficient gelators.[‡]

N-Lauroyl-11-aminoundecanoic acid, **1-H**, represents the simplest entry into the series. Although it has already been reported to act as an amphiphilic molecule forming stable Langmuir–Blodgett films,⁸ its gelation ability has never been mentioned. Yet this compound is a prominent gelator of apolar solvents, such as CCl₄, toluene and *p*-xylene (Table 1). In contrast, the short-chain related derivative, *N*-lauroyl-glycine, was reported⁹ to lack any gelation ability, which was interpreted by the authors as being due to the absence of chirality in the glycine derivative as compared to the *L*-alanine analogue. In the case of the long-chain aminoundecanoic acid, gelation is still effective even though the structure lacks any chiral centre. Toluene gels of **1-H** are optically transparent at low concentration and persist over long periods in a closed vessel (more than one year). Electron microscopy studies of the gels confirm the aggregation of the compound into elongated fibres that entangle to

[†] Present address: LMMB UMR 6114, Université de la Méditerranée, Faculté des Sciences de Luminy, Case 901, 13288 Marseille Cedex 9, France. E-mail: fages@luminy.univ-mrs.fr.

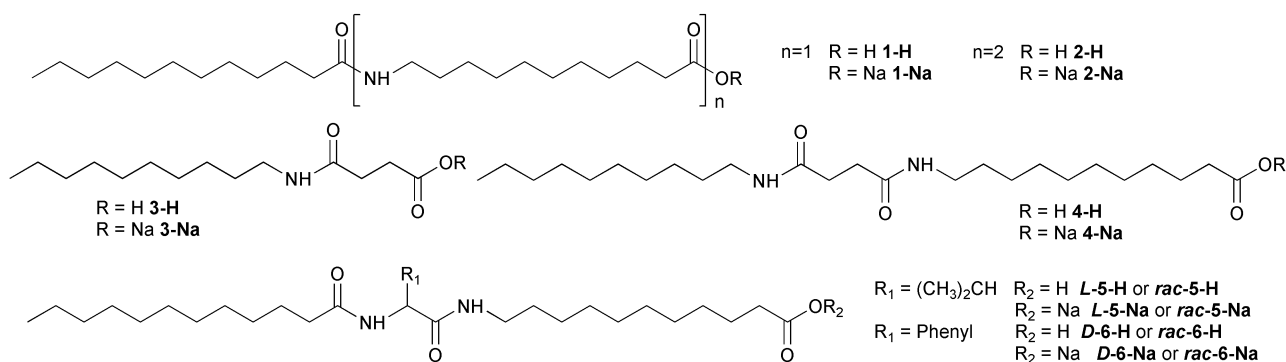


Table 1 Gelation properties of the long-chain amino acid derivatives^a

	1-H	1-Na	2-H	2-Na	3-H	3-Na	4-H	4-Na	L-5-H	L-5-Na	rac-5-H	rac-5-Na	D-6-H	D-6-Na	rac-6-H	rac-6-Na
Decaline	—	—	—	—	—	—	—	—	G(3.3)	G(6.2)	I/E	G(1.5)	G(1.5)	G(4.5)	E	G(0.55)
Toluene	G(7.5)	P	G(3)	—	G(14.1)	P	G(1.1)	I	S	G(10)	P	I	G(16.7)	G(9.1)	P	I
<i>p</i> -Xylene	G(7.2)	P	G(3.5)	—	G(14.2)	P	G(1.3)	I	G(3.5)	G(33.3)	I	I	G(16.7)	G(10)	P	G(0.62)
CH ₂ Cl ₂	I	I	I	—	P	I	I	I	S	I	S	I	I	I	S	I
CCl ₄	G(7.5)	I	I	—	P	I	I	I	—	—	—	—	—	—	—	—
THF	P	P	P	—	G(11.7)	I	G(5.1)	I	G(33.3)	I	S	I	S	G(7.1)	S	I
EtOH	P	P	I	—	S	S	P	P	S	G(16.7)	S	P	P	S	P	P
CH ₃ CN	P	P	I	—	G(3.9)	P	G(4.3)	P	P	P	P	I	P	I	P	I
DMF	S	G(8.5)	S	P ^b	S	G(12.5)	P	G(4.6)	G(10)	G(1.4)	G(100)	G(20)	S	G(8.3)	S	G(16.7)
DMSO	S	G(14.1)	S	P ^b	S	G(15.3)	G(8.5)	P	G(20)	G(3.3)	G(50)	G(12.5)	S	G(8.3)	S	G(9.1)
Water	P	P	P	I	P	S	I	I	S	G(10)	I	G(10)	I	G(8.3)	I	G(12.5)

^a G: gel, in parentheses: minimum gel concentration in g L⁻¹ (gelator/liquid); S: soluble; I: insoluble; P: precipitate; E: emulsion; —: not investigated.

^b Prepared *in situ* with 1 mol eq. NaOH and 1% (v/v) H₂O.

form the typical network features. In particular the results show that elongated fibre formation prevails below the minimum concentration for gel formation (Table 1, Fig. 1), which was also observed by ^1H NMR. The sodium carboxylate derivative of **1-H**, **1-Na**, also shows gelation ability, but only in polar solvents (DMF, DMSO). The diamide linear derivative, **2-H**, which contains two AUDA moieties, displays enhanced gelation properties in aromatic solvents as compared to the monomeric compound **1-H**. Indeed the minimum gelation concentration is observed to decrease by a factor two from **1-H** to **2-H**, which is ascribable to the presence of an extra hydrogen bonding site within the aliphatic chain. A similar effect is also observed when the AUDA unit is tethered to acid **3-H** via an amide functionality to give **4-H**. While the former compound is a rather good gelator, the latter gels aromatic solvents at a 10-fold lower concentration. Interestingly, **4-H** is also able to harden a range of solvents of different polarity as compared to **1-H** and **2-H**. Moreover, the sodium salts **3-Na** and **4-Na** allow the formation of stable gels with solvents that are not gelled by the corresponding neutral acid derivatives.

Not only the minimum gel concentrations but also the gel-to-sol phase transition temperatures are affected when an AUDA unit is introduced into the structure of long-chain amide gelators. An increase in the T_{gel} values is noticed which reflects the increase in the thermal stability of the gels. For example the T_{gel} value for a toluene gel of **2-H** exceeds $100\text{ }^\circ\text{C}$ whereas the gel-to-sol transition is observed at $49\text{ }^\circ\text{C}$ for a toluene gel of **1-H** at the same concentration.

Introduction of an amino acid fragment in the core of *N*-lauroyl-11-aminoundecanoic acid (**1-H**) gives chiral derivatives **L-5-H** and **D-6-H** and their respective Na salts. The combination of a chiral centre and two additional hydrogen-bonding sites profoundly influences the gelation properties. While **1-H** gels 3 of the 11 solvents tested, the Val derivative **L-5-H** is capable of gelating 5 solvents. It is worth noting the shift in gelation preferences from apolar solvents such as toluene and *p*-xylene and CCl_4 (**1-H**) toward highly polar DMF and DMSO (**L-5-H**). However, this property is lost for **D-6-H** which incorporates the aromatic amino acid, α -phenylglycine. Interestingly, **D-6-H** in contrast to **L-5-H** containing an aliphatic amino acid (Val) showed only gelation of the highly lipophilic solvents of the group tested; decaline, toluene and *p*-xylene are gelled by **D-6-H** but not DMF and DMSO (Table 1). Even more dramatic differences can be found by comparison of the gelation properties of **1-Na**, **L-5-Na** and **D-6-Na**; **L-5-Na** and **D-6-Na** are able to gelate 7 of the 11 solvents. These two gelators belong to the rather small group of compounds exhibiting ambidextrous gelating properties. Indeed the apolar decaline, toluene and *p*-xylene can be gelled by the latter compounds as well as the highly polar DMF, DMSO and water. Another intriguing observation is that in contrast to several previous reports,^{9,10} the racemates, **rac-5-Na** and **rac-6-Na** are capable of gelating 4 to 16 times larger volumes of certain solvents than the corresponding pure enantiomers (Table 1). Analysis of the gelation results reveals that pure enantiomers **L-5-H**, **L-5-Na** and **D-6-Na** are more efficient gelators of highly polar and apolar solvents than their racemates but a striking reversal occurs for **rac-5-Na**—decaline—and **rac-6-Na**—decaline and *p*-xylene systems (Table 1). This peculiar

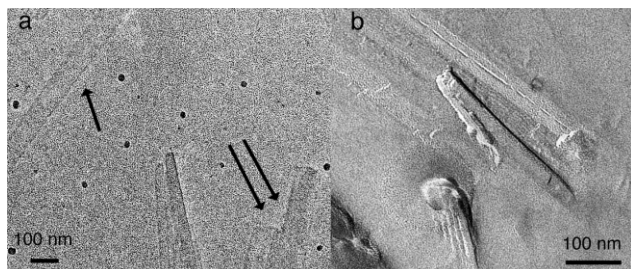


Fig. 1 Electron microscopic studies of toluene solutions of **1-H** revealing the formation of: a) thin individual fibres (3.7 g L^{-1} , diameter: 50 nm , length: up to several microns, estimated thickness: 5 nm) and b) stacks of fibres forming lamellar structures (freeze fracture, 11.3 g L^{-1}).

behaviour remains yet unclear but it is expected that ongoing studies on the organization of racemic and enantiomerically pure gelator molecules within gel fibres will shed more light on this issue. Nevertheless, the reported observations are of high importance for the development of new gelators. They show that gelation preferences and/or gelation efficiency could be strongly influenced by the introduction of chiral amino acid fragments and that in some cases the racemates could be considerably more efficient gelators than pure enantiomers.

In conclusion, the 11-aminoundecanoic acid moiety represents a useful and cheap building-block for the systematic design of highly effective gelators for organic solvents and water. The presented examples clearly illustrate that gelation properties can be tuned by (a) simply adjusting the ionisation state of the terminal carboxylic acid functionality, (b) introducing additional amide hydrogen bonding sites and (c) incorporating a chiral amino acid fragment. The latter possibility allows numerous further variations by using amino acids with different constitutional and conformational characteristics. In particular, understanding the influence of enantiomeric purity on the gelation properties is a challenging task from both fundamental and practical standpoints.

We thank the CNRS, the University Bordeaux I, La Région Aquitaine, and the Deutsche Forschungsgemeinschaft. This work was supported by COST Chemistry Program (COST D11, network 0015/99, <http://www.unil.ch/cost/chem>). Dr P. Schultz is deeply acknowledged for the use of the cryofracturing apparatus at IGBMC UMR 7104, Illkirch, France.

Notes and references

‡ Multi-gram amounts of the compounds described herein were obtained according to simple synthetic steps based on classical peptide coupling procedures. The compounds gave satisfactory spectroscopic and analytical results. Electron microscopy studies were performed according to the procedure described in ref. 2i.

- P. Terech and R. G. Weiss, *Chem. Rev.*, 1997, **97**, 3133; D. J. Abdallah and R. G. Weiss, *Adv. Mater.*, 2000, **12**, 1237; J. H. van Esch and B. L. Feringa, *Angew. Chem., Int. Ed.*, 2000, **39**, 2263.
- (a) E. J. de Vries and R. M. Kellogg, *J. Chem. Soc., Chem. Commun.*, 1993, 238; (b) K. Hanabusa, Y. Matsumoto, T. Miki, T. Koyama and H. Shirai, *J. Chem. Soc., Chem. Commun.*, 1994, 1401; (c) K. Hanabusa, R. Tanaka, M. Suzuki, M. Kimura and H. Shirai, *Adv. Mater.*, 1997, **9**, 1095; (d) S. Bhattacharya, S. N. Ghanashyam and A. R. Raju, *Chem. Commun.*, 1996, 2101; (e) N. Mizoshita, T. Kutsuna, K. Hanabusa and T. Kato, *Chem. Commun.*, 1999, 781; (f) S. Bhattacharya and Y. Krishnan-Ghosh, *Chem. Commun.*, 2001, 185; (g) H. M. Willemsen, T. Vermonden, A. T. M. Marcelis and E. J. R. Sudhölter, *Eur. J. Org. Chem.*, 2001, 2329; (h) R. P. Lyon and W. M. Atkins, *J. Am. Chem. Soc.*, 2001, **123**, 4408; (i) R. Schmidt, M. Schmutz, A. Mathis, G. Decher, M. Rawiso and P. Mésini, *Langmuir*, 2002, **18**, 7167.
- G. Wang and A. D. Hamilton, *Chem. Commun.*, 2003, 310; F. M. Menger and K. L. Caran, *J. Am. Chem. Soc.*, 2000, **122**, 11679; J. Schneider, C. Messerschmidt, A. Schulz, M. Gnade, B. Schade, P. Luger, P. Bombicz, V. Hubert and J.-H. Fuhrhop, *Langmuir*, 2000, **16**, 8575; M. Suzuki, M. Yumoto, M. Kimura, H. Shirai and K. Hanabusa, *Chem. Commun.*, 2002, 884.
- J. Makarevic, M. Jokic, B. Peric, V. Tomisic, B. Kojic-Prodic and M. Zinic, *Chem. Eur. J.*, 2001, **7**, 3328; C. Boettcher, B. Schade and J.-H. Fuhrhop, *Langmuir*, 2001, **17**, 873.
- G. Mieden-Gundert, L. Klein, M. Fischer, F. Vögtle, K. Heuzé, J.-L. Pozzo, M. Vallier and F. Fages, *Angew. Chem., Int. Ed.*, 2001, **40**, 3164.
- Gelators based on α,ω -alkyldenediamines: K. Tomioka, T. Sumiyoshi, S. Narui, Y. Nagaoka, A. Iida, Y. Miwa, T. Taga, M. Nakano and T. Handa, *J. Am. Chem. Soc.*, 2001, **123**, 11817.
- N. A. Jones, P. Sikorski, E. D. T. Atkins and M. J. Hill, *Macromolecules*, 2000, **33**, 4146.
- R. Popovitz-Biro, K. Hill, E. Shavit, D. J. Hung, M. Lahav, L. Leiserowitz, J. Sagiv, H. Hsiung, G. R. Meredith and H. Vanherzle, *J. Am. Chem. Soc.*, 1990, **112**, 2498.
- X. Luo, B. Liu and Y. Liang, *Chem. Commun.*, 2001, 1556.
- K. Hanabusa, H. Kobayashi, M. Suzuki, M. Kimura and H. Shirai, *Colloid Polym. Sci.*, 1998, **276**, 252; K. Hanabusa, K. Okui, K. Karaki, M. Kimura and H. Shirai, *J. Colloid Interface Sci.*, 1997, **195**, 86; S. Bhattacharya, S. N. Ghanashyam Acharya and A. R. Raju, *Chem. Commun.*, 1996, 2101.