Self-Assembly of Non-Biological Polymeric Strands Undergoing Enforced Helical Self-Organization

by **Jean-Louis Schmitt** and **Jean-Marie Lehn***

ISIS-ULP-CNRS UMR 7006, 8, allée Gaspard Monge, BP 70028, F-67083 Strasbourg cedex
(phone: 0390245145; fax 0390245140; e-mail: lehn@isis.u-strasbg.fr)

Dedicated to Professor *Dieter Seebach*

The polycondensation of a dihydrazino-pyrimidine (**5** and **6**) with a pyrimidine-dicarbaldehyde (**7** and **8b**) provides an efficent access to helical polymeric strands based on the formation of hydrazone connections between the pyrimidine groups. The folding into a helical structure is enforced by the helicity codon defined by the (hydrazone–pyrimidine) sequence. The polymers obtained have been characterized by mass spectrometry, indicating molecular weights up to *ca.* 12000 Da. Electronic spectra display specific absorption and emission features. These helical polymers present a core diameter of *ca.* 20 Å, a pitch of 3.5 Å, and, for a molecular weight around 9000 Da, a height of *ca.* 42 Å with 12 turns. The self-assembled helical polymers obtained represent stable frameworks for the lateral attachment of functional residues in a helical disposition. Such entities may possess a range of novel chemical as well as biological properties.

Introduction. – The precise control of structure generation determines function and is, thus, of prime importance in biology as well as in materials science and nanotechnology on both the molecular and the supramolecular levels. It rests on self-organization processes [1–3], leading to complex molecular and supramolecular architectures, and is directed both by the structural and conformational information encoded in the molecule, acting through the patterns of non-covalent intermolecular interactions between components. Adequate programming of the generation of a well-defined structure requires the orchestration of multiple interactional features, thus directing a molecular strand to spontaneously adopt a specific geometry by a *self-folding* process. It requires a detailed analysis of the geometrical and interactional features that determine the generation of a given three-dimensional architecture from a biological or synthetic molecular strand [2] as output of a suitably instructed, programmed chemical system [3][4]. This is, in particular, the case for the highly complex factors and pathways involved in protein folding [5][6].

Supramolecular architectures result from the self-assembly of the molecular components under the control of patterns of intermolecular, non-covalent interactions. Similarly, it may be possible to generate precise molecular architectures by self-assembly from suitable components connected through reversible covalent bonds. Such control requires the recognition and implementation of *structuration codons* on the molecular and supramolecular levels. Thus, specific H-bonding patterns [7–9] may yield either linear [10] or circular [11][12] supramolecular assemblies. The folding of a molecular strand into a well-defined geometrical entity is a problem whose importance is matched by its complexity. This applies of course first to protein folding, but also to

synthetic, non-biological molecular strands, whose arrangement into a given geometrical pattern has been subject of intense investigation in recent years [2]. One may note in particular that 'folding diseases' (*e.g.*, *Alzheimer* and prion diseases) result from conformational states and changes of proteins [13].

Principles for the Generation of Self-Folding Helical Strands. – Helical molecular entities are of special interest in view of their characteristic geometrical features as well as their role in biology, where H-bonding, stacking interactions, and conformational effects contribute to the stabilization of the α-helix of polypeptides and the double helix of DNA. Helical folding of a chain may be driven by stacking or electrostatic interactions and solvophobic effects [2][14–17], as well as by H-bonding (for recent examples see, *e.g.* [18–21]). In our laboratory, specific arrays of H-bonding sites have been used to induce helicity in heterocyclic-polyamide strands [22][23], which may dimerize into double helices by stacking of two helical strands [22][24]. H-bonding interaction with an appropriate template has also been used to induce folding of a molecular strand [25]. The induction of helicity by helical programing [2][26] is, thus, being actively investigated. On the other hand, helical self-organization of multisubunit ligand strands into inorganic double helices, the helicates, is induced by binding of metal ions of appropriate coordination geometry [3][27].

In an another approach, in an earlier work from our group, it has been shown that suitable sequences of directly connected heterocyclic units impose a specific geometry on a polyheterocyclic strand by virtue of the marked conformational preference for a *transoid* orientation around the connecting bonds. In particular, the (2,4′)-pyridine-pyrimidine (py-pym) sequence represents a *helicity codon* that has been shown to enforce helical wrapping of a molecular $(\text{py-pym})_n$ strand [28–30]. Control of the geometrical properties may be achieved by appropriate modifications. Thus, replacing the pyrimidine group by a pyridazine unit leads to helices of larger diameter that stack into extended fibers [31]. Furthermore, it was shown that the pyridine group could be replaced by an isomorphic hydrazone (hyz) unit, which preserves the strong preference for a *transoid* orientation in the (hyz-pym) sequence [32].

As a consequence, imine formation, *e.g.*, in hydrazones, provides a very efficient synthesis of helical strands by molecular self-assembly through amine–carbonyl condensation. Furthermore, since the reaction is reversible, the entities generated may, in principle, undergo the exchange and selection processes characteristic of dynamic combinatorial chemistry [33][34]. Imine functionalities have recently been introduced into *m*-phenylene-ethynylene foldamers to connect the subunits [35][36]. A logical extension of our earlier work was to replace all pyridine groups in a $(\text{py-pym})_n$ strand by hydrazone units so as to form $(\text{hyz-pym})_n$ strands representing helical oligomers and polymers. A process such as the formation of a helical superstructure *via* hydrazone formation combines a number of features of general interest: *1*) the generation of an oligomeric or a polymeric strand by molecular self-assembly through imine formation; *2*) the isomorphic pyridine → hydrazone replacement, which results in a facile synthetic procedure to give efficient, fast, and controlled access to the products, and to allow stepwise condensation to yield discrete oligomers as well as polycondensation to polymeric materials, in this case of helical type; *3*) the control of the folding of a molecular strand through interactional patterns defining structuration codons; in this

case, a helicity codon, but other geometries may be induced; *4*) the reversibility of the self-assembly reaction, conferring constitutional dynamic capacity [1] and generating folded structures, in this case, carbonyl–amine (hydrazine) condensations yielding dynamic molecular helices capable, in principle, of incorporating, decorporating, and exchanging components; *5*) within the general framework of dynamic chemistry [1][37], the generation of dynamic materials, in particular, dynamic polymers ('dynamers') [38][39]; presenting reversibility, healing, adjustability (adaptation) through reversible covalent connections, conferring to molecular entities and the dynamic features of supramolecular materials [1][33][36–40].

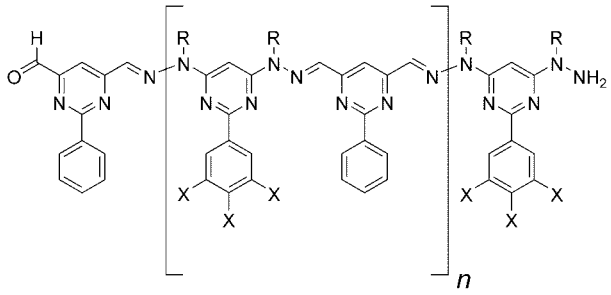
We have reported earlier the synthesis of a number of oligomeric molecular strands based on $(hyz\text{-}pym)_n$ units ($n = 1-9$; up to 10 hyz groups) and described their helical structures, displaying up to 3⅓ turns [41]. We now present the synthesis, characterization, and some properties of the polymers **1**-H, **1**-Me, **2**-H, **2**-Me, **3**-Me, and **4**-Me generated from the polycondensation of the dihydrazino-pyrimidines **5** and **6** with the pyrimidine-dicarbaldehydes **7** and **8b**.

Synthesis of the Polymeric Strands 1 and 2. – Two methods were employed for the synthesis of the polymers **1**–**4** depending upon whether the monomer used was a dihydrazino-pyrimidine (**5**-H and **6**-H) or a bis(methylhydrazino) derivative (**5**-Me and **6**-Me). In the case of the dihydrazino compounds, the conditions for polymer formation were optimal when a one-to-one equiv. of **5**-H or **6**-H, and dicarbaldehyde **7** or **8b** in a $CHCl_3$/MeOH solution were treated with a catalytic amount of AcOH. In the case of the bis(methylhydrazino)-pyrimidines **5**-Me and **6**-Me, the presence of AcOH and MeOH were unnecessary.

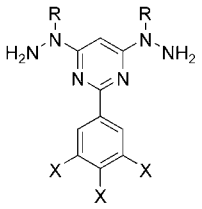
Characterization and Properties of the Helical Strands 1–4. – The polymers **1** and **2** are yellow solids, stable over several months upon storage below 0°. The *N*-methylated polymers **1**-Me and **2**-Me were soluble in a wide range of organic solvents such as $CHCl_3$, CH_2Cl_2, THF, and DMSO. The unmethylated polymers **1**-H and **2**-H, on the other hand, were only poorly soluble in $CHCl_3$/MeOH 9:1 mixture.

Analysis of the Polymers **1** *and* **2** *by Mass Spectrometry.* Extensive investigations of the polymers **1** and **2** were performed by MALDI-TOF and FAB mass spectrometry. The spectra revealed the presence of species between 1000- and 12000-Da molecular weight, displaying regular mass distribution over the whole domain (*Figs. 1* and *2*). These molecular weights cover a range of oligomers to polymers from 6 to 50 residues. Mass peaks were present at alternating intervals corresponding, respectively, to polymers differing by a bis(methylhydrazino)-pym unit or a diformyl-pym unit (see *Figs. 1* and *2*). The chains may be terminated either by two bis(methylhydrazino)-pym units, two diformyl-pym units, or by one unit of each type.

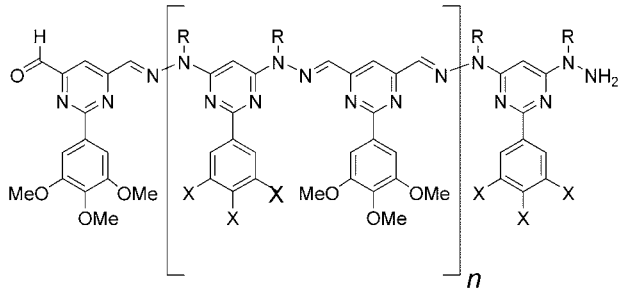
Interestingly, the FAB mass spectra gave mass peaks displaying association of the different polymers with Na^+ and K^+ ions present in the matrix. The chains terminated by amine functional groups were found to associate preferentially with Na^+, while those terminated by aldehyde groups bound preferentially K^+. Macrocycles were detectable in all mass spectra, but only those containing 4 and 6 heterocyclic rings and an equivalent amount of both monomers.



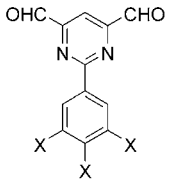
1-H R = H X = H
1-Me R = Me X = H
2-H R = H X = MeO
2-Me R = Me X = MeO



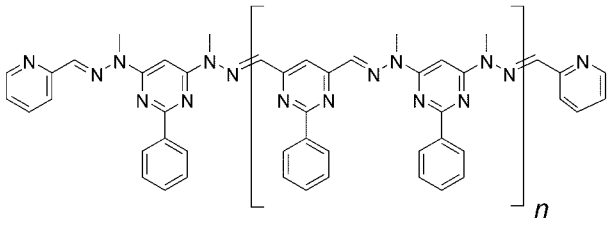
5-H X = H
5-Me X = Me
6-H X = MeO
6-Me X = MeO



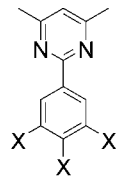
3-Me R = Me X = H
4-Me R = Me X = MeO



7 X=H
8b X=MeO



9-A *n* = 1
9-B *n* = 2



8a X = MeO

[1]H-NMR Spectra of the Polymers **1**-*Me and* **2**-*Me.* The polymers **1**-Me and **2**-Me gave [1]H-NMR spectra displaying extensive line-broadening even at higher temperatures. They could not be used for structural characterization, and it was not possible to unambiguously assign the NOE cross-peaks for determining interproton interactions.

Electronic Absorption and Fluorescence Spectra of the Polymers **1**-*Me and* **2**-*Me.* The electronic absorption and the fluorescence spectra of the polymer **1**-Me are shown in *Figs. 3* and *4*, respectively, together with corresponding spectra of the oligomers **9a**

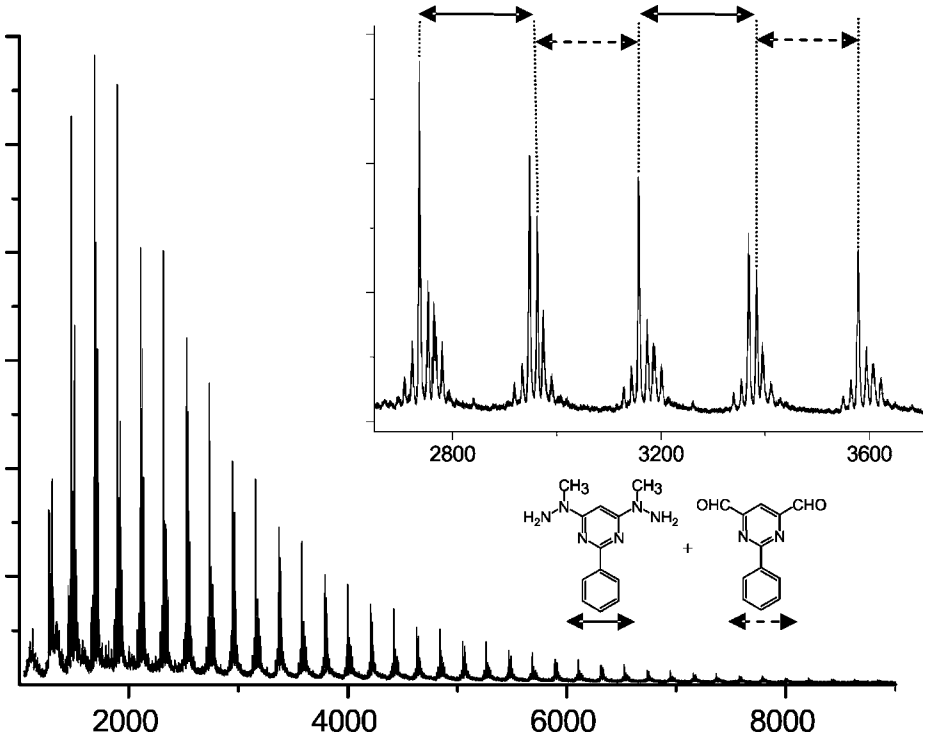


Fig. 1. *MALDI-TOF Mass spectrum of polymer* **1**-*Me*

and **9b**, described earlier [41], for comparison purposes. The UV absorption spectrum of polymer **1**-Me presents two broad bands with maxima around 300 and 260 nm, the latter being somewhat more intense. The first may arise from the terminal pyridines, and the second from the pyrimidine and/or hydrazone units. Such an assignment would agree with the relative intensities of the bands observed at similar wavelengths in the oligomers **9**, which display a higher pyridine-to-pyrimidine ratio than the polymers, *i.e.*, a more intense band at 300 than at 260 nm [41].

The emission spectra display more distinctive features. Thus, the polymer **1**-Me shows a strong, very broad (200-nm-wide) and featureless emission centered at *ca.* 470 nm, as compared to *ca.* 430 nm for the oligomers **9** (*Fig. 4*). The shift to longer wavelength by *ca.* 30 nm in the polymer with respect to the longest oligomer **9b** is in line with earlier results on helical (py-pym) strands, indicating such a shift with increasing length of the strand [29][30]. This is in agreement with a more intense excimer emission as the number of stacked pyrimidines increases with the chain length in the polymers.

Helical Structure and Geometric Features of the Polymers **1**–**4**. On the basis of the helical form of the oligomers **9** and related compounds [41], one may confidently assign a helical structure to the polymers **1**–**4**. All spectral data available agree with such a formulation. Thus, polycondensation of the dihydrazino-pyrimidines **5** and **6**, and pyrimidine-dicarbaldehydes **7** and **8b** yields polymers presenting a strongly enforced

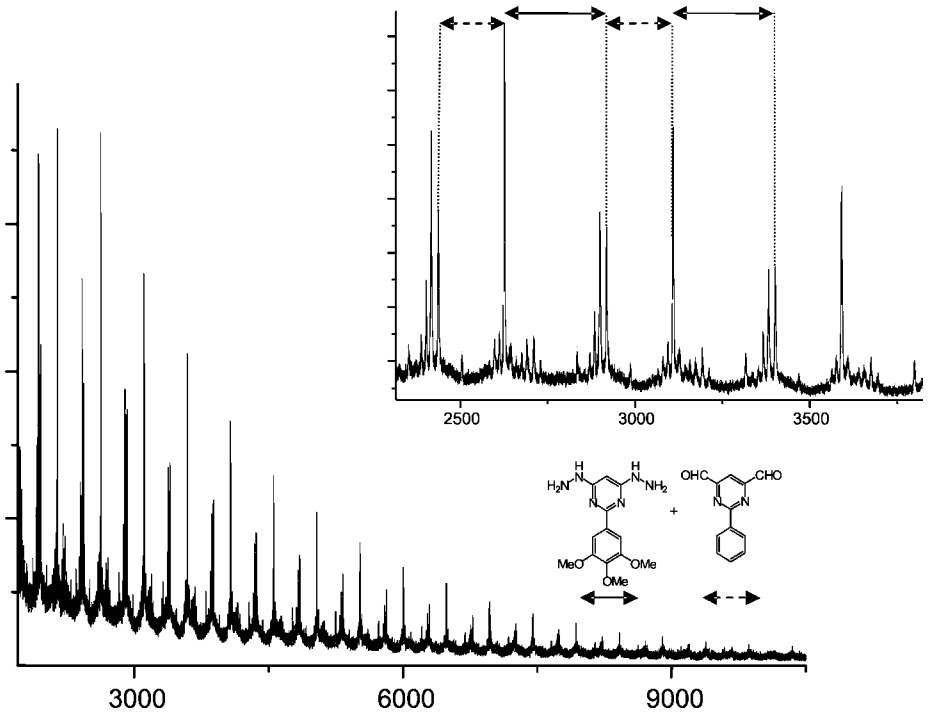


Fig. 2. *MALDI-TOF Mass spectrum of polymer* **2**-*H*

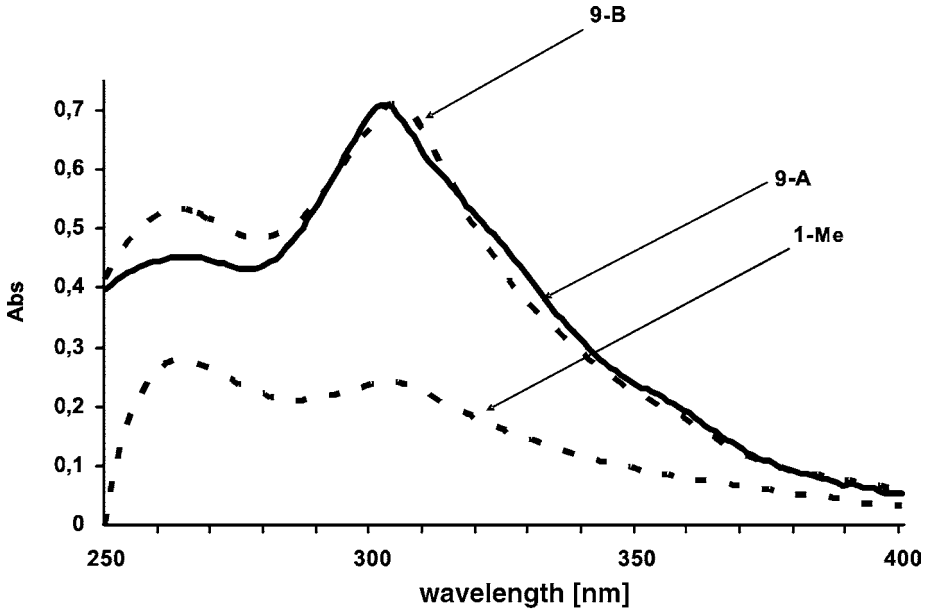


Fig. 3. *Electronic absorption spectra of the oligomers* **9a**, **9b**, *and of the polymer* **1**-*Me*

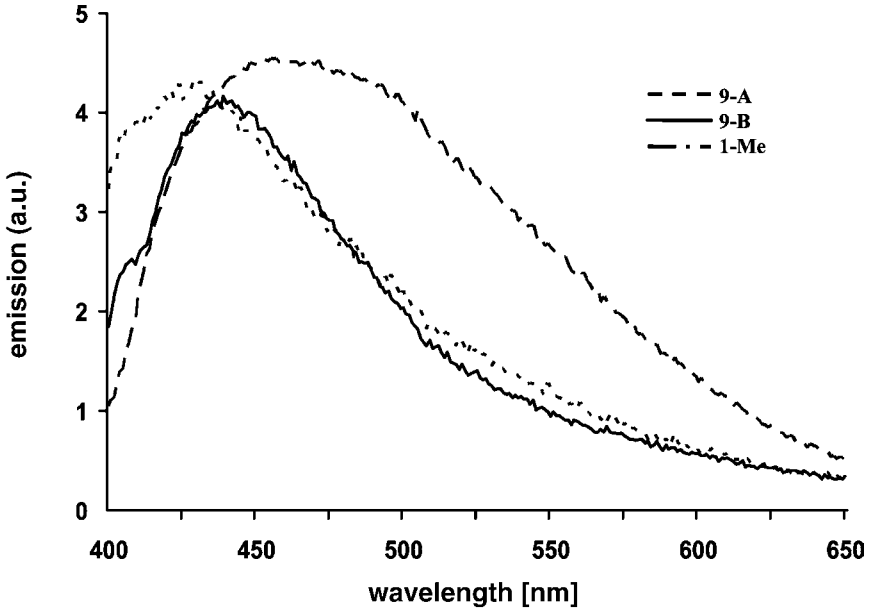


Fig. 4. *Fluorescence emission spectra of the oligomers* **9a**, **9b**, *and of the polymer* **1**-*Me in* CH_2Cl_2 *under excitation at 310 nm*

helical structure, as represented by **10**. A long polymeric strand of **1**-Me of molecular weight *ca.* 9000 Da, as found in the mass spectrum, is expected to correspond to a helix containing *ca.* 12 turns. Using the pitch of 3.5 Å found in the crystal structure of the oligomers **9** [41], the core of this helix may be inscribed in a cylinder with a diameter of 20 Å and a height of 42 Å, as shown in *Fig. 5*.

Physicochemical Properties of Polymers **1**–**4**. Molecular strands generated by multiple hydrazine–carbonyl condensations may, in principle, be dynamic, in view of the reversibility of the reaction. Such reversibility would make the strands chemically unstable, but allow, potentially, the exchange of the components forming the strand, a property characteristic of constitutionally dynamic systems [1][4][38–40]. In the case of the oligomers **9** as well as of the polymer **1**-Me, addition of the bis(methylhydrazino)-trimethoxyphenyl-pyrimidine **6**-Me (in various organic solvents, in absence or presence of acid) did not lead to any exchange. This result indicates that the tight stacking within the helices, as seen in the crystal structures of the related oligomers [41], hinders access of an external reagent to the hydrazone functions, thus precluding component exchange. As a result, the self-assembled helices obtained are chemically resistant. Replacing the hydrazone groups by imines might allow component exchange, rendering the helical structures dynamic. Such studies are being persued.

Conclusion. – The present results extend the earlier work on the induction of helical folding to polymeric strands on the basis of a helicity codon defined by the (hyz-pym) sequence. Hydrazone formation allows the facile self-assembly of such extended helical entities. Their chemical stability, resulting probably from the tight packing within the

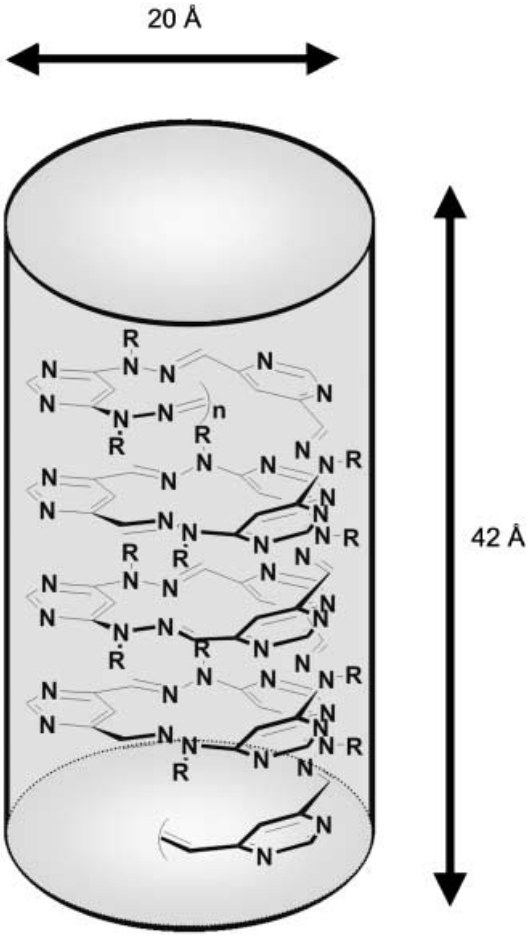


Fig. 5. *Schematic representation of the core helix of the polymeric helical strands* **1**–**4** *inscribed in a cylinder of 20-Å diameter.* The height indicated corresponds to a polymer of *ca.* 9000 Da presenting 12 turns; substituents on the helix omitted for clarity.

spiral, makes them attractive frameworks for the helical arrangement of lateral functional groups. On the other hand, it may be possible to introduce reversibility in the self-assembly process by appropriate modification of the connecting groups, leading to dynamic helical strands capable of assembling, dissociating, and exchanging components, thus opening helical folding processes to constitutional dynamic chemistry [1].

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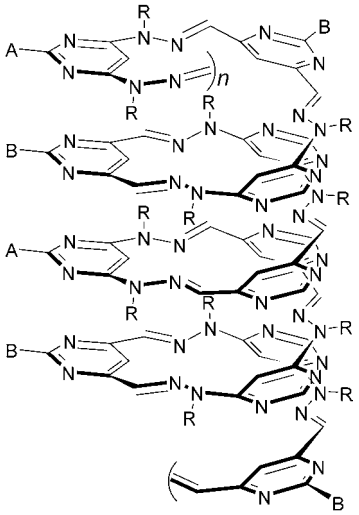

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Experimental Part

General. TLC: *Polygram Sil G/UV$_{254}$* pre-coated plastic sheets. Flash chromatography (FC): 230–400-mesh silica-gel particles supplied by *Merck*. M.p.: *Büchi B-540* melting-point apparatus, uncorrected. ^{1}H (200 or 400 MHz) and ^{13}C-NMR spectra (50 or 100 MHz) were recorded on *Bruker AC-200* or *Avance-400* spectrometers, respectively; $CDCl_3$ as solvent, unless otherwise noted, chemical shifts δ are in ppm with a residual solvent ^{1}H peak as reference. Electron-ionization, fast-atom-bombardment mass spectra (FAB-MS) were recorded by the Service d'Analyse de l'Université Louis Pasteur; MALDI-MS was carried out on a *Bruker Autoflex* or on a *Perseptive Biosystems Voyager Pro DE* with dithranol as matrix.

4,6-Dimethyl-2-(3,4,5-trimethoxyphenyl)pyrimidine (**8a**). A soln. of 3,4,5-trimethoxybenzamidine hydrochloride (4 g, 16.2 mmol), acetylacetone (2.9 ml, 27.5 mmol), an K_2CO_3 (7.12 g, 51.5 mmol) in 25 ml of H_2O was stirred for 30 min and then left to stand for 3 d. The white precipitate was filtered, washed with H_2O, dissolved in CH_2Cl_2, and dried ($MgSO_4$) to yield **8a** (2.5 g, 56%). White solid. ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.76 (*s*, 2 H); 6.92 (*s*, 1 H); 4.01 (*s*, 6 H); 3.93 (*s*, 3 H); 2.55 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 166.6; 163.5; 153.2; 133.6; 117.8; 105.3; 60.9; 56.2; 32.41. FAB-MS: 275.2 (100, $[M+H]^+$).

2-(3,4,5-Trimethoxyphenyl)pyrimidine-4,6-dicarbaldehyde (**8b**). A soln. of **8a** (0.50 g, 1.8 mmol) and SeO_2 (0.44 g, 0.40 mmol) was refluxed in dioxane (15 ml) for 1 h under an Ar atmosphere. The hot soln. was filtered and cooled, the solvent was then removed under reduced pressure, and the residue was purified by chromatography (SiO_2; $CHCl_3$) to give **8b** (50 mg, 9%). Yellow solid. M.p. 165°. ^{1}H-NMR ($CDCl_3$, 400 MHz): 10.20 (*s*, 2 H); 8.10 (*s*, 1 H); 7.91 (*s*, 2 H); 4.02 (*s*, 6 H); 3.96 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 192.1; 160.2; 155.9; 153.6; 109.6; 105.8; 105.30; 61.0; 56.3. FAB-MS: 303.1 (100, $[M+H]^+$).

Synthesis of the Polymeric Strand **1**–**4**. The same general procedures have been used for the synthesis of the six polymeric strands **1**–**4**, with a slight difference in the conditions for the *N*-H and the *N*-Me derivatives. Typical procedures are described below.

Polymer **1**-*H*. A soln. of *2-phenylpyrimidine-4,6-dicarbaldehyde* (**7**; 50 mg, 0.23 mmol) and *4,6-dihydrazino-2-(3,4,5-trimethoxyphenyl)pyrimidine* (**6**-H; 72 mg, 0.23 mmol) in 20 ml of $CHCl_3$/EtOH 70:30 (*v*/*v*) was stirred at r.t. for 4 d. The soln. was concentrated to 10 ml, MeOH was added, and the precipitate was filtered and washed with MeOH.

Polymer **1**-*Me*. A soln. of **7** (50 mg, 0.23 mmol) and *4,6-bis(1-methylhydrazino)-2-(3,4,5-trimethylphenyl)-pyrimidine* (**5**-Me; 56 mg, 0.23 mmol) in 20 ml of $CHCl_3$ was stirred at r.t. for 4 d. The soln. was concentrated to 10 ml, MeOH was added, and the precipitate was filtered.

REFERENCES

[1] J.-M. Lehn, *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4763.
[2] D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes, J. S. Moore, *Chem. Rev.* **2001**, *101*, 3893.
[3] J.-M. Lehn, 'Supramolecular Chemistry – Concepts and Perspectives' VCH, Weinheim, Germany, **1995**.
[4] J.-M. Lehn, *Chem.–Eur. J.* **2000**, *6*, 2097.
[5] C. M. Dobson, A. Sali, M. Karplus, *Angew. Chem., Int. Ed.* **1998**, *37*, 868.
[6] Special Issue on Protein Folding, *Acc. Chem. Res.* **1998**, *31*, 697.
[7] M. Krische, J.-M. Lehn, *Struct. Bonding* **2000**, *94*, 3.
[8] J. R. Fredericks, A. D. Hamilton, in 'Comprehensive Supramolecular Chemistry', Vol. 9, Eds. J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn, Pergamon Press, Oxford, 1996, Chapt. 16, p. 565 – 594.
[9] E. E. Simanek, X. Li, I. S. Choi, G. M. Whitesides, in 'Comprehensive Supramolecular Chemistry', Vol. 9, Eds. J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn, Pergamon Press, Oxford, 1996, Chapt. 17, p. 595 – 621.
[10] J.-M. Lehn, M. Mascal, A. DeCian, J. Fischer, *J. Chem. Soc., Perkin Trans. 2* **1992**, *2*, 461.
[11] A. Marsh, M. Silvestri, J.-M. Lehn, *Chem. Commun.* **1996**, 1527; M. Mascal, N. M. Hext, R. Warmuth, M. H. Moore, J. P. Turkenburg, *Angew. Chem., Int. Ed.* **1996**, *35*, 2204.
[12] M. Suarez, J.-M. Lehn, S. C. Zimmerman, A. Skoulios, D. Heinrich, *J. Am. Chem. Soc.* **1998**, *120*, 9526.
[13] J. C. Socchettini, J. W. Kelly, *Nature Rev. Drug Discovery* **2002**, *1*, 267; C. M. Dobson, *Nature Rev. Drug Discovery* **2003**, *2*, 154.
[14] L. Brunsveld, E. W. Meijer, R. B. Prince, J. S. Moore, *J. Am. Chem. Soc.* **2001**, *123*, 7978.
[15] J. C. Nelson, J. G. Saven, J. S. Moore, P. G. Wolynes, *Science* **1997**, *277*, 1793.
[16] S. Lahiri, J. L. Thompson, J. S. Moore, *J. Am. Chem. Soc.* **2000**, *122*, 11315.
[17] R. P. Cheng, W. F. DeGrado, *J. Am. Chem. Soc.* **2002**, *124*, 11564.
[18] B. Gong, *Chem.–Eur. J.* **2001**, *7*, 4337.
[19] D. Seebach, J. V. Schriber, P. I. Arvidsson, J. Frackenpohl, *Helv. Chim. Acta* **2001**, *84*, 271; P. J. Gee, F. A. Hamprecht, L. D. Schuler, W. F. van Gunsteren, E. Duchardt, H. Schwalbe, M. Albert, D. Seebach, *Helv. Chim. Acta* **2002**, *85*, 618.
[20] S. H. Gellman, *Acc. Chem. Res.* **1998**, *31*, 173; K. D. Stigers, M. J. Soth, J. S. Nowick, *Curr. Opin. Chem. Biol.* **1999**, *3*, 714.
[21] D. Yang, Y.-H. Zhang, N.-Y. Zhu, *J. Am. Chem. Soc.* **2002**, *124*, 9966.
[22] V. Berl, I. Huc, R. G. Khoury, M. J. Krische, J.-M. Lehn, *Nature (London)* **2000**, *407*, 720.
[23] V. Berl, I. Huc, R. G. Khoury, J.-M. Lehn, *Chem.–Eur. J.* **2001**, *7*, 2798.
[24] V. Berl, I. Huc, R. G. Khoury, J.-M. Lehn, *Chem.–Eur. J.* **2001**. *7*, 2810.
[25] V. Berl, M. J. Krische, I. Huc, J.-M. Lehn, M. Schmutz, *Chem.–Eur. J.* **2000**, *6*, 1938.
[26] A. E. Rowan, R. J. M. Nolte, *Angew. Chem., Int. Ed.* **1998**, *37*, 63.
[27] C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005; M. Albrecht, *Chem. Rev.* **2001**, *101*, 3457; E. C. Constable, *Tetrahedron* **1992**, *48*, 10013.
[28] G. S. Hanan, J.-M. Lehn, N. Kyritsakas, J. Fischer, *J. Chem. Soc., Chem. Commun.* **1995**, 765.
[29] D. M. Bassani, J.-M. Lehn, G. Baum, D. Fenske, *Angew. Chem., Int. Ed.* **1997**, *36*, 1845; D. M. Bassani, J.-M. Lehn, *Bull. Soc. Chim. Fr.* **1997**, *134*, 897.
[30] M. Ohkita, J.-M. Lehn, G. Baum, D. Fenske, *Chem.–Eur. J.* **1999**, *5*, 3471.
[31] L. A. Cuccia, E. Ruiz, J.-M. Lehn, J.-C. Homo, M. Schmutz, *Chem.–Eur. J.* **2002**, *8*, 3448.
[32] K. M. Gardinier, R. G. Khoury, J.-M. Lehn, *Chem.–Eur. J.* **2000**, *6*, 4124.
[33] J.-M. Lehn, *Chem.–Eur. J.* **1999**, *5*, 2455.
[34] G. R. L. Cousins, S. A. Poulsen, J. K. M. Sanders, *Curr. Opin. Chem. Biol.* **2000**, *4*, 270.
[35] K. Oh, K.-S. Jeong, J. S. Moore, *Nature (London)* **2001**, *414*, 889.
[36] T. Nihinaga, A. Tanatani, K. Oh, J. S. Moore, *J. Am. Chem. Soc.* **2002**, *124*, 5934; D. Zhao, J. S. Moore, *J. Am. Chem. Soc.* **2002**, *124*, 9996.
[37] J.-M. Lehn, in 'Supramolecular Science: Where It Is and Where It Is Going', Eds. R. Ungaro, E. Dalcanale, Kluwer Academic Publishers., 1999, 287 – 304.
[38] J.-M. Lehn, W. G. Skene, in preparation; Provisional Patent Application, 2002, 60/392, 308.
[39] J.-M. Lehn, *Polym. Int.* **2002**, *51*, 825.
[40] S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem., Int. Ed.* **2002**, *41*, 898.
[41] J.-L. Schmitt, M. Stadler, J.-M. Lehn, *Helv. Chim. Acta* **2003**, *86*, 1598.

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