Helicity Coding: Programmed Molecular Self-Organization of Achiral Nonbiological Strands into Multiturn Helical Superstructures: Synthesis and Characterization of Alternating Pyridine – Pyrimidine Oligomers

Masakazu Ohkita,[a] Jean-Marie Lehn,*[a] Gerhard Baum,[b] and Dieter Fenske[b]

Abstract: Alternating pyridine – pyrimidine oligomers **1**, **2**, and **3**, composed of nineteen, twenty one, and twenty seven heterocycles, respectively, have been synthesized in stepwise fashion and characterized. Examination of their ^{1}H NMR spectra revealed that these achiral nonbiological oligomers organize spontaneously into multiturn helical structures **1A** – **3A** in solution, as indicated by marked upfield shifts of the aromatic protons coupled with distinct NOE effects. In view of their potential electron-acceptor properties compounds **1** – **3** also represent coiled wires of nanometric lengths, up to about 90 Å for **3** in its extended form. The helical structure has been confirmed for **1** in the solid state by X-ray crystallography; a chiral channel arrangement involving only one helical enantiomer was found despite of the lack of chiral center in the strand. The oligomers exhibit a broad structureless fluorescence with a large Stokes shift, attributable to intramolecular pyridine excimer emission resulting from the helical ordering. Variable-temperature ^{1}H NMR experiments revealed that the oligomers exist as equilibrating mixtures of right-handed and left-handed helices. The barrier for helical handedness reversal was found to be independent on the length of the strand; two- (**6**), three- (**1**), and four-turn (**3**) helices showed comparable free energies of activation. Based on these observations, a stepwise folding mechanism involving two perpendicularly twisted pyridine – pyrimidine units in the transition states may be proposed for the helicity inversion processes. The present results together with earlier work indicate that the pyridine – pyrimidine sequence may be considered as a *helicity codon*, enforcing the formation of helical structures on the basis of intramolecular structural information.

Keywords: helical structures · nitrogen heterocycles · noncovalent interactions · pyridine-pyrimidine helicity codon · self-organization

Introduction

The design of molecular species capable of undergoing self-organization into a well-defined structure opens the way to the spontaneous but controlled generation of highly complex chemical architectures. This *molecular* self-organization process is directed by the structural and conformational information encoded in the molecule and operated through *intramolecular* noncovalent interactions, just in the same way as *supramolecular* self-organization operates through *intermolecular* interactions.[1]

Molecular self-organization into helical architectures is found for biological macromolecules, as in the case of the α-helix of polypeptides and the double helix of DNA, where hydrogen bonding, stacking interactions and hydrophobic effects contribute to the formation and stabilization of such biological helices.[2] The design of nonbiological species that spontaneously organize into helical architectures is of considerable interest in view of their relation to life sciences as well as of their potential applications in materials science, nanotechnology and optical and electronics devices.[3, 4]

The spontaneous generation of helical chemical entities requires the encoding of specific structural and conformational information within the molecules. We have recently designed a new structural motif for helicity induction based on three encoding features: 1) an alternating pyridine – pyrimidine (py – pym) sequence, 2) linkage at specific positions, and 3) the preference for a *transoid* conformation around the single bonds between the heterocyclic units. The preference of the *transoid* conformation may be attributed to electrostatic repulsion between the nitrogen dipoles and steric repulsion between the CHs in the *cisoid* conformation as well as weak CH···N hydrogen bonding in the *transoid* form. Strands of this type **4**[5] and **6**[6] have, indeed, been found to adopt one-

[a] Prof. Dr. J.-M. Lehn, Dr. M. Ohkita
Laboratoire de Chimie Supramoléculaire
ISIS, Université Louis Pasteur
4, rue Blaise Pascal, F-67000 Strasbourg (France)
Fax: (+33) 3-88-41-10-20
E-mail: lehn@chimie.u-strasby.fr

[b] G. Baum, Prof. Dr. D. Fenske
Institut für Anorganische Chemie der Universität
Karlsruhe (Germany)

  0947-6539/99/0512-3471 $ 17.50+.50/0

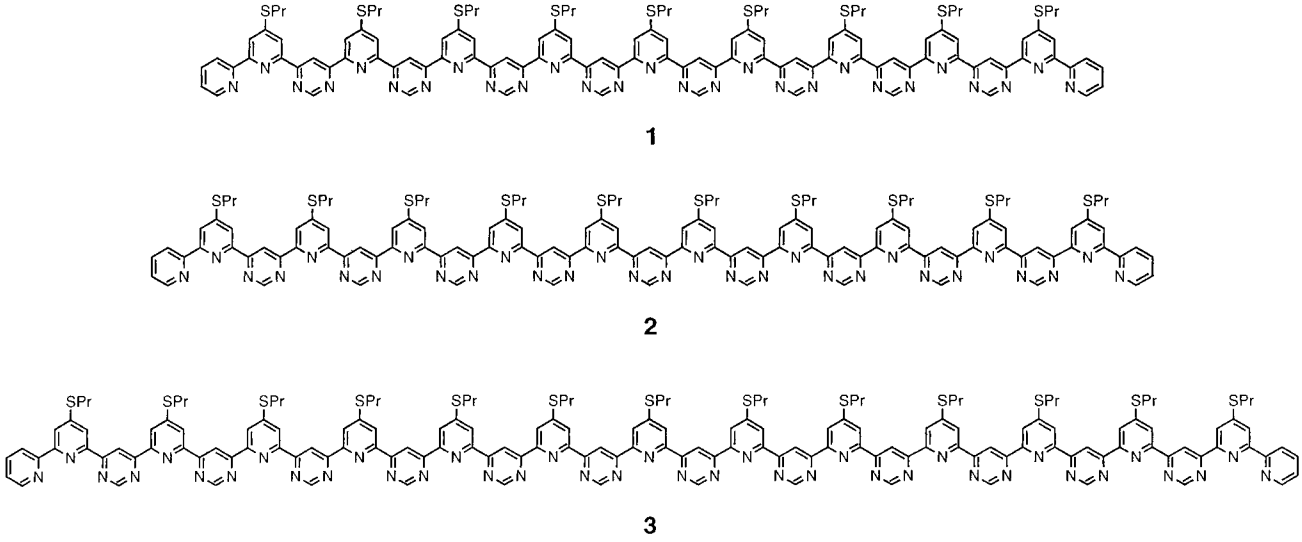


Figure 1. Structure of the alternating pyridine–pyrimidine oligomeric strands **1**, **2**, **3** in linear representation. SPr refers to S*n*Pr groups.

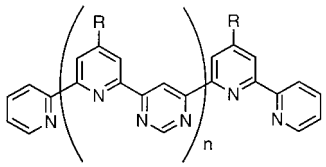
turn and two-turn helical structures, respectively, both in solution and in the solid state. We have further developed this approach to the extended oligomers **1**, **2**, and **3**, composed of nineteen, twenty one, and twenty seven heterocycles, respectively (Figure 1). In this paper we describe the details of the synthesis of **1**–**3** and their self-organization into mutiturn helical structures including X-ray crystallographic investigations. In addition, **1**–**3** may be regarded as extended polytopic ligands presenting respectively 9, 10, and 13 tridentate complexation sites which may allow the construction of large metallosupramolecular assemblies, such as multimetallic racks, ladders, or grids[7].

Abstract in Japanese:

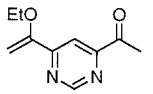
交互ピリジン-ピリミジンオリゴマー１-３が段階的に合成され、その特性が明らかにされた。プロトン核磁気共鳴スペクトルにおける芳香族プロトンの顕著な高磁場シフトと明確な核オーバーハウザー効果によって、これらのオリゴマーが溶液中で自発的に多重らせん構造に組織化することが示された。化合物１の結晶中でのらせん構造がX線結晶構造解析により確認された。また、このストランドは、不斉中心を持たないにもかかわらず、一方のらせん対掌体のみから成るキラルなチャンネル構造を与えた。オリゴマー１-３は大きくストークスシフトした、幅広く、振動構造を持たない蛍光を示した。これらは、そのらせん配列に起因する分子内ピリジンエキシマー発光に帰属される。プロトン核磁気共鳴スペクトルの温度可変実験により、オリゴマー１-３は右巻きと左巻きらせん構造の平衡混合物として存在することが示された。このらせん反転に対する障壁はストランドの長さに依存せず、二回転（６）、三回転（１）、および四回転（３）らせん化合物は反転に対して同程度の活性化自由エネルギーを示した。この観察結果に基づいて、らせん反転過程に対して、遷移状態で二つの垂直にねじれたピリジン-ピリミジン部分を含む段階的折りたたみ機構が提案された。

Results and Discussion

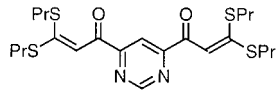
Synthesis of the strands 1–3: The preparation of **1**–**3** was carried out by two different routes based on the repetitive Potts' synthesis of 2,6-disubstituted pyridine units (see



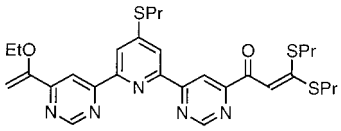
4 n = 2, R = H
5 n = 2, R = SPr
6 n = 5, R = SPr



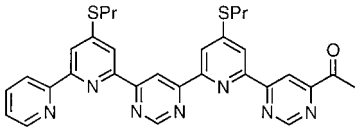
7



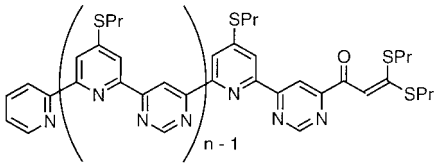
8



9



10

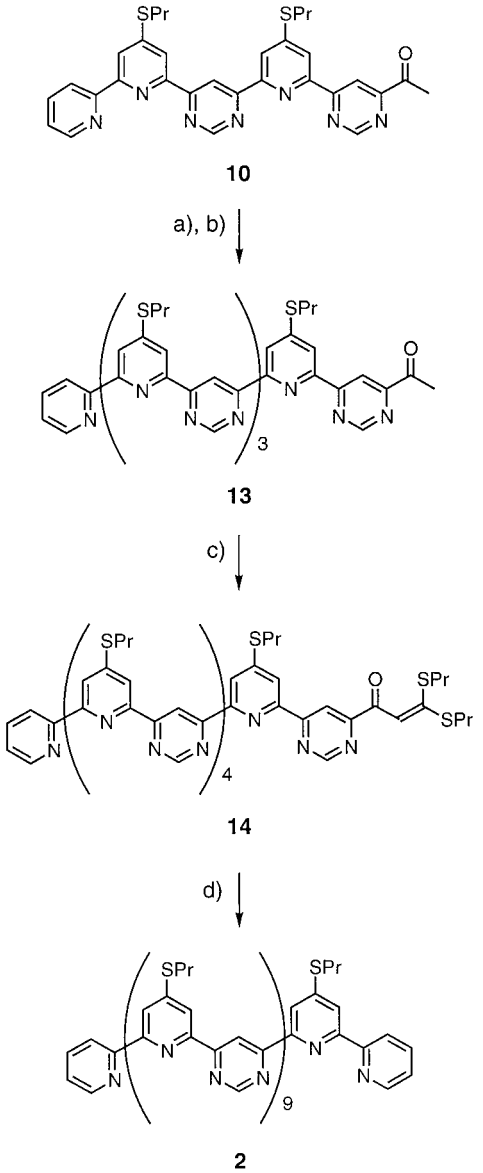


11 n = 1
12 n = 3

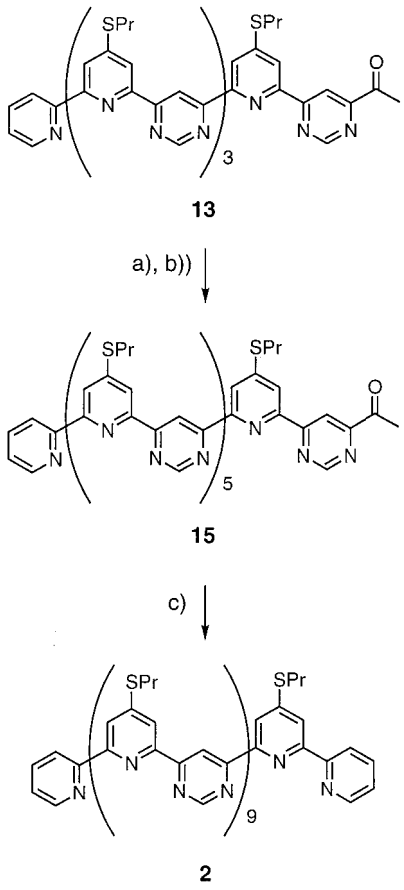
0947-6539/99/0512-3472 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 12

Schemes 1–3).[8] Initially the synthesis of oligomer **2** was attempted by using the method previously reported for the lower homologue **6**.[6] However, simple extension of this approach, in which the strand was constructed by starting from the terminal pyridine units and combining the two subunits thus prepared in the final step, was found not to be suitable for the preparation of longer strands, so that modification in the synthetic strategy was required. We therefore developed an alternative approach based on the repetitive twofold reaction of a bifunctional central unit with two small building blocks to avoid the unfavorable steric and conformational effects found in the initial sequence.

The starting building blocks **7**–**12** were prepared by following the previously reported method.[6] In the initial approach (Scheme 1), ketone **10** was treated with a homologating building block **9**, having a Michael acceptor group and a protected ketone moiety, to produce ketone **13** in 58% yield after hydrolysis. Monoaddition of **13** to the bis(Michael acceptor) **8** afforded the Michael acceptor **14** in 51% yield. Reaction of **13** with **14**, however, led to the formation of a large amount of tarry material and provided the desired oligomer **2** in only about 1% yield at best under the several reaction conditions examined. Since both **13** and **14** should have more than one-turn helical structures, it is possible that the reaction sites in both building blocks are shielded by the helical backbone, resulting in their low reactivities. The pyridine ring forming step from the 1,5-diketone intermediate may also be hindered by the two large substituents present in **13** and **14**. Consistent with these rationalizations, the yield of **2** could be improved to some extent by using a combination of larger and smaller building blocks, i.e. **15** and **12** (Scheme 2), but was still low (7%).

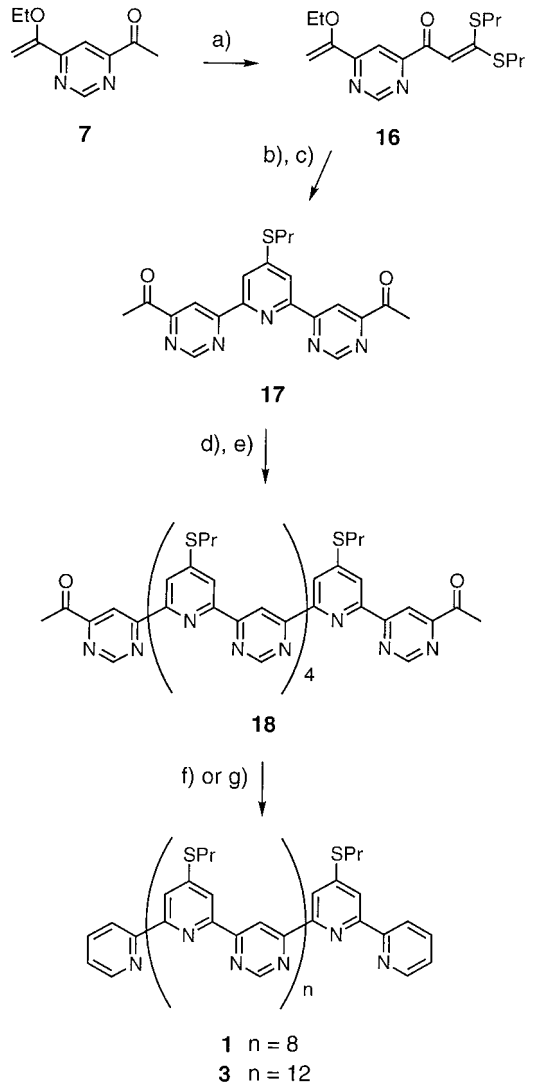


Scheme 1. a) *t*BuOK, **9**, THF, then NH_4OAc, AcOH (62%); b) HCl_{aq}, acetone (93%); c) *t*BuOK, **8**, THF, then NH_4OAc, AcOH (51%); d) *t*BuOK, **13**, THF, then NH_4OAc, AcOH (1%); SPr refers to S*n*Pr.



Scheme 2. a) *t*BuOK, **9**, THF, then NH_4OAc, AcOH (27%); b) HCl_{aq}, acetone (80%); c) *t*BuOK, **12**, THF, then NH_4OAc, AcOH (7%); SPr refers to S*n*Pr.

The multitude of reaction steps coupled with unsatisfactory yields in the above preparations prompted us to exploit a second approach and substantial improvement could be achieved (Scheme 3). Thus, successive treatment of **7** with sodium hydride, carbon disulfide, and propyl iodide in DMSO afforded the corresponding α-oxoketene dithioacetal **16** in 68% yield. This was treated with **7** to give diketone **17** in 36% yield after hydrolysis. Twofold condensation of **17** with **9** gave the homologated diketone **18** in 28% yield after hydrolysis. Reaction of **18** with the Michael acceptor **11** afforded oligomer **1**, possessing 19 heterocycles, in 34% yield while



Scheme 3. a) NaH, CS_2, PrI, DMSO (68%); b) *t*BuOK, **7**, THF, then NH_4OAc, AcOH; c) HCl_{aq}, acetone (36%, 2 steps); d) *t*BuOK, **9**, THF, then NH_4OAc, AcOH; e) HCl_{aq}, acetone (25%, 2 steps); f) *t*BuOK, **11**, THF, then NH_4OAc, AcOH (34% for **1**); f) *t*BuOK, **13**, THF, then NH_4OAc, AcOH (5% for **3**), SPr refers to S*n*Pr.

reaction of **18** with the extended Michael acceptor **12** produced oligomer **3**, possessing 27 heterocycles, in 5% yield. The yield of 34% for the twofold reaction generating **1** is noteworthy because it is equivalent to about a 60% yield for each condensation reaction, much higher than the 1% and 7% yields obtained for preparing **2** by the previous approaches (Schemes 1 and 2). Since the size and possibly the reactivity of **9** are similar to those of **11**, further homologation of **18** using **9** might allow the preparation of even longer strands.

The oligomers **1**–**3** were isolated as colorless powders after extensive chromatography on alumina followed by reprecipitation from chloroform/acetone. They are soluble in chloroform, slightly soluble in dichloromethane and THF, but insoluble in ether, methanol, acetone, and acetonitrile. The fast atom bombardment (FAB) mass spectra of **1**–**3** clearly indicate their molecular ion peaks with consistent isotope patterns.

^{1}H NMR studies of 1–3: The ^{1}H NMR spectrum of **1** is rather simple, consistent with its symmetric nature, and shows twenty one signals in the aromatic region (Figure 2a); eight doublets ($^4J = 1.8$ Hz) for the trisubstituted pyridine protons, eight doublets ($^5J = 1.2$ Hz) for the pyrimidine protons, one singlet for the central trisubstituted pyridine protons, and four multiplets for the terminal pyridine protons. Similarly, the ^{1}H NMR spectra of **2** and **3** display the expected signals (Figures 2b and 2c).

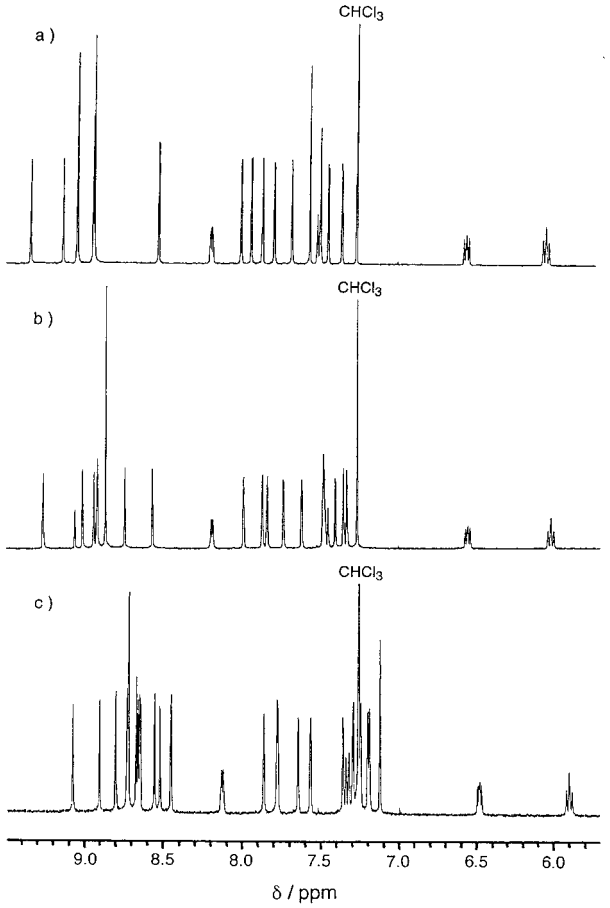


Figure 2. 400 MHz ^{1}H NMR spectra (aromatic region) of (a) **1**, (b) **2**, and (c) **3** in $CDCl_3$.

The oligomers **1**–**3** exhibit characteristic features of helix formation in their ^{1}H NMR spectra. Thus, marked upfield shifts are observed for the terminal pyridine proton resonance of H-C4 because of the shielding effect of the aromatic rings lying directly above and below this proton in the helical conformation: $\delta = 7.64$ for pyridine, $\delta = 6.03$ for **1**, $\delta = 6.01$ for **2**, and $\delta = 5.90$ for **3** in $CDCl_3$. Consistent with helical ordering, significantly different chemical shifts are observed for the protons in each thiopropyl groups; for example, methyl protons in **1** are observed at $\delta = 1.11$ (6H), 1.17 (6H), 1.24 (6H), 1.35 (6H), and 1.41 (3H). Moreover, distinct NOE effects are observed between the protons oriented towards the interior of the helix, for example the pyrimidine protons H-C(5) and the terminal pyridine protons H–C3, as exemplified by the ROESY spectrum of **3** (Figure 3, only pyrimidine protons shown).

0947-6539/99/0512-3474 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 12

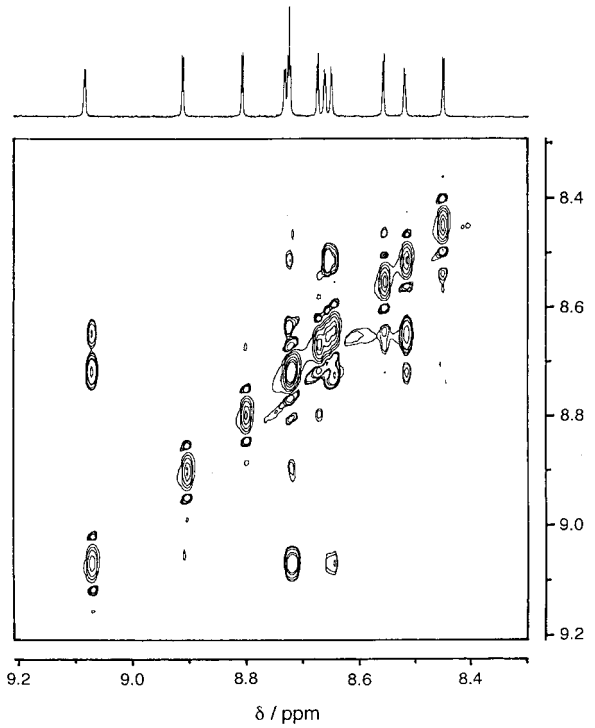
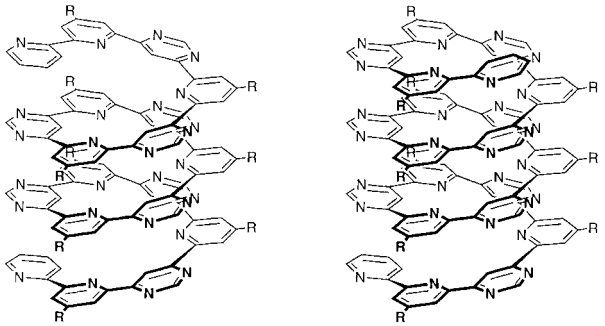


Figure 3. ^{1}H NMR ROESY spectrum (pyrimidine protons) of **3** in $CDCl_3$.

These observations closely resemble those made for the previously established helices of the lower homologues **4** and **6**. Consequently, the extended strands **1**–**3** may be considered to also adopt in solution a helical conformation represented schematically by **1A**–**3A**. Further support for the helical ordering is provided by the comparison of the chemical shifts

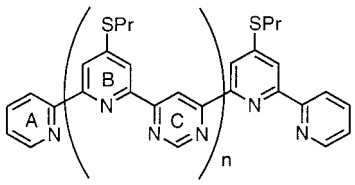


1A R = S*n*Pr **2A**

of the aromatic protons in the series of py–pym strands (Table 1 and Figure 4); indeed, progressive upfield shifts with increasing strand length are observed, consistent with the cumulative effect of an increasing number of stacked aromatic units as the number of turns of the helices increases.

Crystal structures of strand 1: Crystals of **1** suitable for X-ray structure determination were obtained by slow diffusion of acetonitrile into a solution of **1** in chloroform at room temperature. The molecular structure and crystal packing of **1** are presented in Figures 5 and 6. The unit cell contains two

Table 1. Average ^{1}H NMR chemical shifts (in ppm) of aromatic protons in $CDCl_3$.



Compound	*n* (Rings)	Turn(s)	Ring-A	Ring-B	Ring-C	Average
-	1 (5)[6]	0	8.16	8.41	9.56	8.43
5[6]	2 (7)	1	7.50	8.31	9.54	8.22
6[6]	5 (13)	2	7.24	7.96	9.27	8.20
1	8 (19)	3	7.07	7.67	8.98	8.06
3	12 (27)	4	6.96	7.43	8.70	7.89

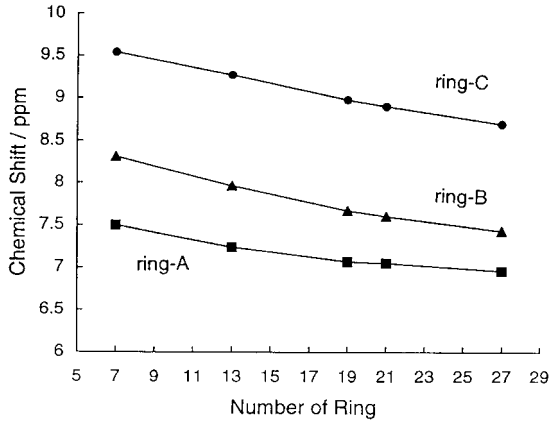
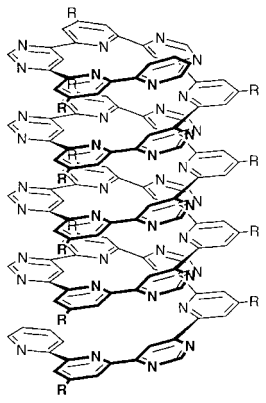


Figure 4. Representation of the change of the average ^{1}H NMR chemical shifts of the aromatic protons of compounds **1**–**6** as a function of number of heterocyclic rings (see also Table 1).



3A

molecules of helical shape in only one enantiomeric form, together with two chloroform molecules. The helical molecules are stacked on each other in the unit cell and the long axis of the unit cell coincides with that of the helical molecule itself (Figure 6). Accordingly, chiral channel structures are generated in the solid state from the achiral linear strand **1** by the self-organization process. The py–pym torsional angles lie within about $11 \pm 3^\circ$. The helical structure of **1** possesses a helical pitch of 3.75 Å and an interior void of about 2 Å diameter (considering a projection in a plane and taking into account the van der Waals radii of diagonally located N and C–H sites).

Structural features of strands 1–3: Compounds **1**, **2**, and **3** have in their fully extended state a length of about 60, 70, and 90 Å, respectively. The spectroscopic and crystal data indicate that they spontaneously wrap up into helical forms of type **1A**–**3A**. These may thus be considered to represent *coiled molecular wires* of nanometric size, possessing potential

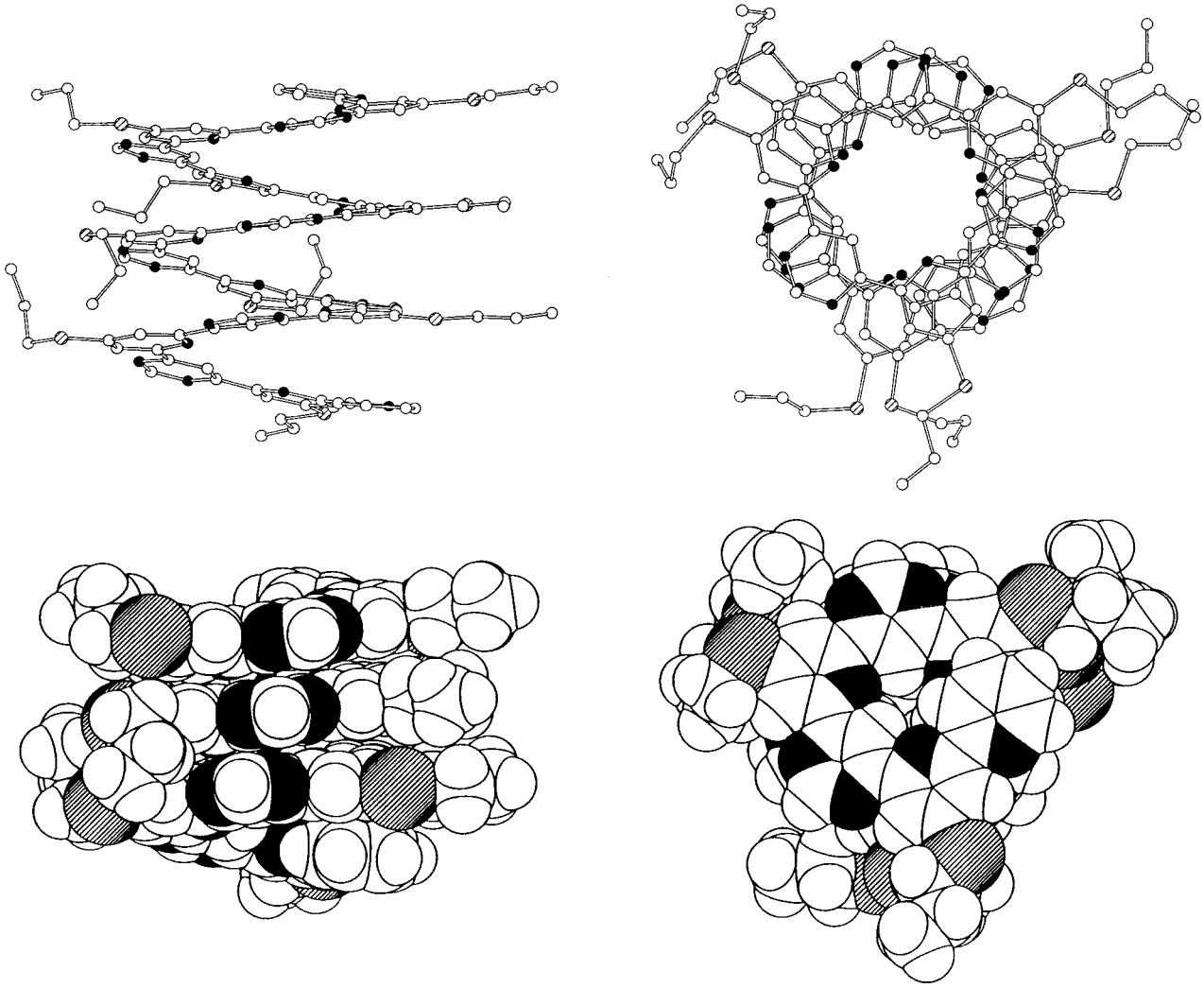


Figure 5. . Crystal structure of **1**; view perpendicular to (left) and along (right) the axis of the helix in ball-and-stick (top) and space-filling (bottom) representations.

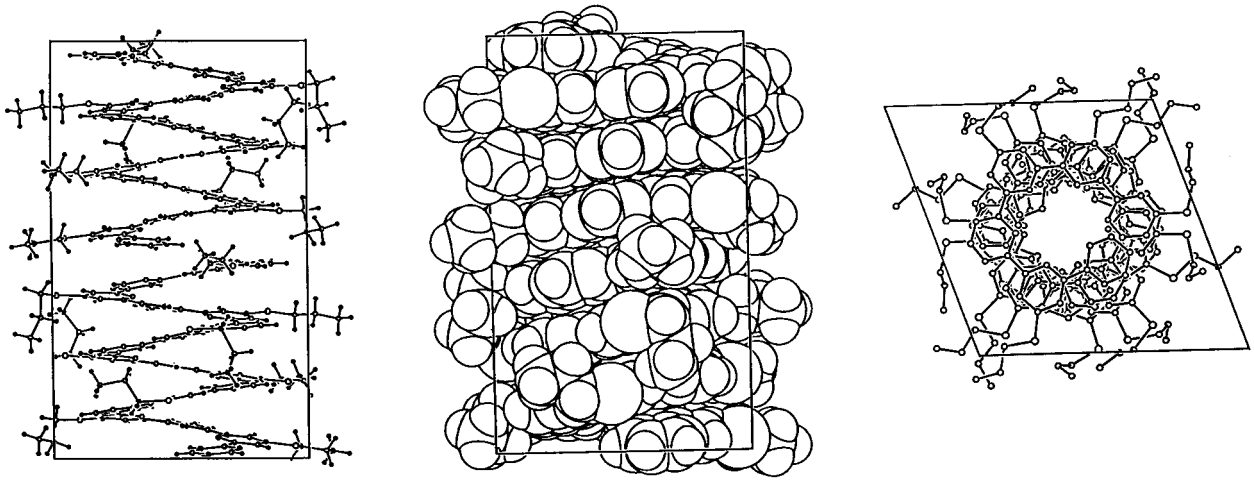


Figure 6. Representation of the packing of **1** in the unit cell. View: perpendicular to the axis of the helix, left (ball-and-stick) and center (space filling); along the axis, right (ball-and-stick).

electron-acceptor properties in view of the nature of their component subunits. These species, or derivatives thereof, may display intriguing electronic features, in particular with respect to linear molecular wires, which have been subject of much interest in recent years. Partial or full uncoiling may be brought about by external stimuli such as protonation or metal ion coordination, making possible a reversible interconversion between the coiled and extended linear forms.

0947-6539/99/0512-3476 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 12

Furthermore, the organized helical structure also provides a way to position peripheral substituents in well-defined spatial arrangement relative to one another along the coiled strand. Such a property is reminiscent of the structural framework offered by the DNA double helix itself.

Absorption and fluorescence emission spectra: Since the present helical self-organization process leads to stacking of heteroaromatic rings, spectroscopic examination of intramolecular interactions between these chromophores is of interest. As shown in Figure 7, the electronic absorption spectra of

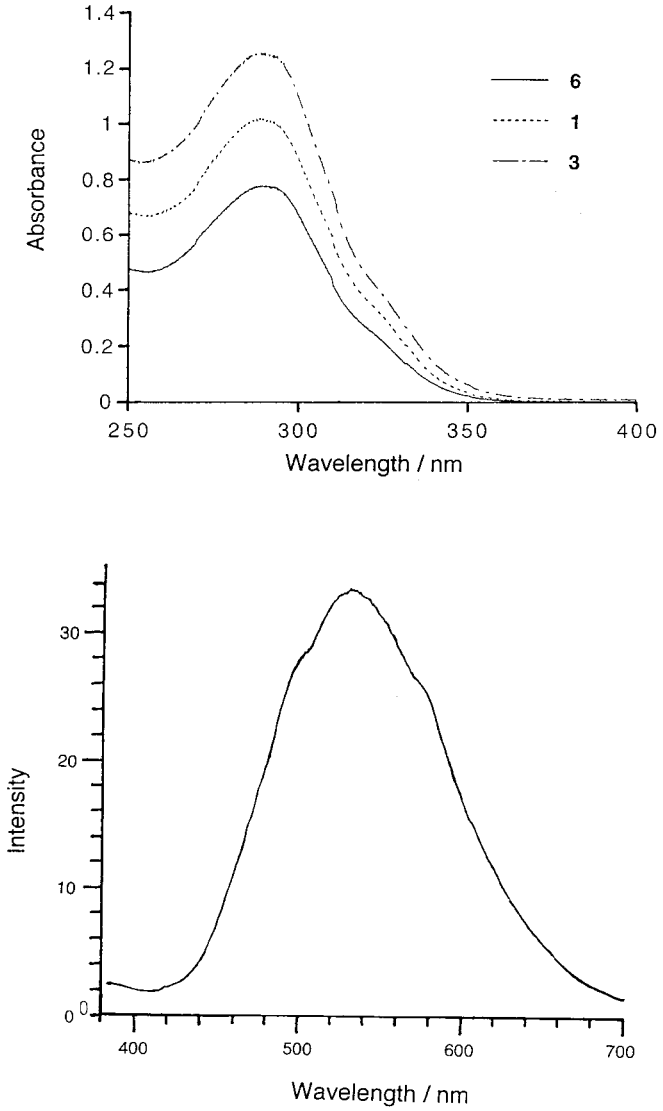


Figure 7. Top: Electronic absorption spectra of **1**, **3** and **6** in dichloromethane (5×10^{-6} M). Bottom: Fluorescence emission spectrum of **1** in dichloromethane (1×10^{-5} M).

the two-turn (**6**), three-turn (**1**), and four-turn (**3**) py–pym strands in dichlorometane exhibit absorption maxima at the same wavelength (289 nm) and similar end absorption extending to about 365 nm; no significant red-shift was observed. On the other hand, the absorption coefficients of **6**, **1**, and **3** at 289 nm are 156000, 203000, and 251000, respectively, and thus reduction in optical absorption intensity was observed with respect to what one might expect on the basis of the number of heterocyclic rings. Hypochromic effects are commonly seen in DNA, RNA, and other polymers[9] and the observed hypochromism also reflects the helical ordering and stacking of the chromophores. The lack of significant red-shift may be rationalized in terms of rather loose helical conformations of **1**–**3** in solution. In this respect, 2,2′-bipyridine has been reported to adopt a nonplanar *transoid* conformation with an interplanar angle of about 20° in organic solvents, whereas it exists in a planar *transoid* conformation in the solid state.[10]

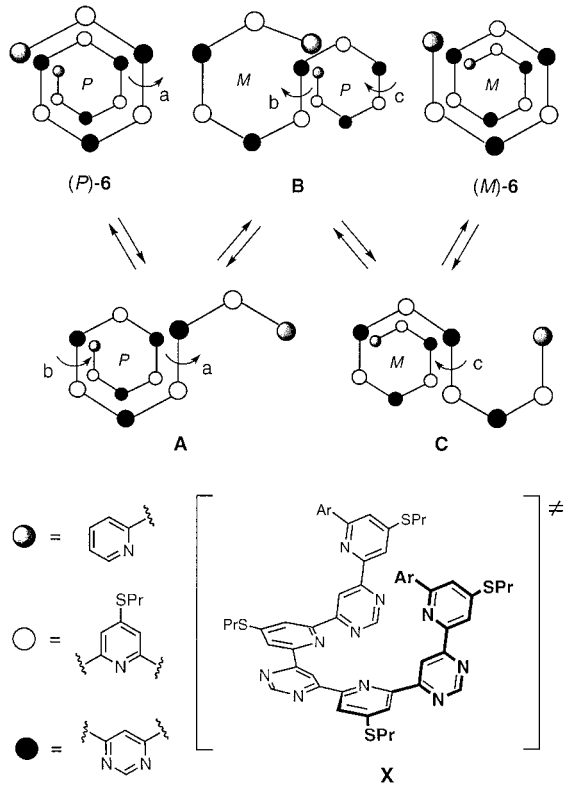
Electronic interactions between the chromophores through intramolecular π-stacking were also observed in the fluorescence spectra of **1** and **3**. The two-turn strand **6** has been reported to show a characteristic fluorescence emission at 540 nm that was not observed for the one-turn strand **5**, which showed simple pyridine-like emission at 400 nm.[6] Similarly, excitation of the three-turn oligomer **1** at 280 nm in dilute dichloromethane resulted in a broad structureless emission centered at 532 nm (Figure 7). The four-turn oligomer **3** also exhibited similar fluorescence but at slightly shorter wavelength (519 nm) under the same recording conditions. These characteristic emissions with large Stokes shifts may be attributed to intramolecular pyridine excimer-like emission resulting from the overlapping of pyridine residues in the multiturn helical conformations. The smaller Stokes shifts observed for the emissions of **1** and **3** as compared to that of **6** could be due to lesser mobilities of the longer strands. Intermolecular pyridine excimer emission at 550 nm has been reported for poly(pyridine-2,5-diyl).[11]

Dynamic behavior and helicity interconversion of the helical strands: In achiral solution, py–pym strands should generate a mixture of equal amounts of right-handed (*P*) and left-handed (*M*) helices, which may interconvert with each other. Examination of such exchange process is of considerable interest because the factors affecting the exchange process should contribute to the formation and stabilization of the helical structure, and thus to the helical self-organization process itself. Since the interconversion between enantiomeric helices results in the exchange of the diastereotopic α-methylene protons of the S-propyl side chains, these become magnetically equivalent when the interconversion is fast enough on the NMR time scale. Accordingly, the exchange process was examined by variable-temperature ^{1}H NMR (400 MHz) experiments.

Decoupling of the β-methylene protons in **1** at 300 K resulted in the observation of the α-methylene protons as singlets, indicating that **1** exist as a rapidly equilibrating mixture of enantiomeric helical forms at this temperature. The singlets split into AB quartets as the temperature was lowered and the maximum splitting was observed at 220 K with a chemical shift difference of $\Delta\nu = 23.9$ Hz and a coupling constant of $J_{A,B} = 12.4$ Hz. The coalescence temperature was determined to be $T_c = 250$ K. With these values, an exchange rate constant at coalescence $k_c = 85\ s^{-1}$ at 250 K was calculated, which leads to the free energy of activation of $\Delta G^{\ddagger}_c = 12.4$ kcal mol^{-1} (52.0 kJ mol^{-1}). In a similar manner, $\Delta\nu = 23.9$ Hz, $J_{A,B} = 12.4$ Hz, and $T_c = 275$ K were determined

for **3**, giving $k_c = 86\ s^{-1}$ and $\Delta G^{\neq}_c = 13.6$ kcal mol^{-1} (57.1 kJ mol^{-1}) at coalescence. Values of $k_c = 85\ s^{-1}$ and $\Delta G^{\neq}_c = 12.3$ kcal mol^{-1} (51.6 kJ mol^{-1}) at $T_c = 251$ K have been reported for **6**.[6b]

For the interconversion of *P* and *M* helices, two alternative mechanisms, a global wrap–unwrap process and a stepwise folding through a partially unwrapped form, may be considered. With the global mechanism, longer strands must contain more *cisoid* conformations in their unwrapped forms and thus the barrier should significantly increase with the length of the strand. However, the fact that comparable activation free energies were observed for **6** (12.3 kcal mol^{-1}), **1** (12.4 kcal mol^{-1}), and **3** (13.6 kcal mol^{-1}) is inconsistent with this mechanism. Examination of molecular models suggested a stepwise folding mechanism which is illustrated by the conversion of (*P*)-**6** to (*M*)-**6** represented in Scheme 4. Thus,



Scheme 4. Stepwise folding mechanism for the helicity inversion of **6**.

rotation around bond a in (*P*)-**6** would give a partially opened intermediate **A** and concomitant rotation around bonds a and b in **A** would produce an intermediate **B**. Further rotation around of bonds b and c in **B** would afford an intermediate **C** which would give (*M*)-**6** by rotation around bond c. Intermediates **A**–**C** interconvert through a common transition state structure **X** possessing two perpendicular py–pym units. Since the residual helical moieties in the **X** species are directed toward the outside, this mechanism would be applicable not only for **6** but also for longer strands **1** and **3**. A perpendicularly twisted 2,2′-bipyridine has been calculated to be about 29 kJ mol^{-1} higher in energy than its planar *transoid* form,[12] so that an activation free energy of about 58 kJ mol^{-1} would be expected for the interconversion process, assuming that a py–pym unit presents a similar energy difference between its perpendicular and planar *transoid* conformations. This value is in good agreement with the experimentally observed barriers for **6** (51.6 kJ mol^{-1}), **1** (52.0 kJ mol^{-1}), and **3** (57.1 kJ mol^{-1}). Consequently, this *stepwise folding mechanism* is plausible for the *helicity inversion* process of the helical strands **1**–**3** and **6** and can probably be extended to other polyheterocyclic strands.

Conclusion

We have synthesized and characterized alternating py–pym oligomers **1**-**3** that spontaneously organize into multiturn helical superstructures **1A**–**3A** both in solution and in the solid state. Within the framework of molecular devices, they may be considered to represent coiled molecular wires that may potentially be decorated by peripheral substituents in well-defined relative arrangements. Interestingly, the achiral linear strand **1** has been found to afford chiral crystals containing only one helical enantiomer. Thus, the dynamic equilibrium between the two helical enantiomers offers the possibility to induce absolute helicity through crystallization.

The present results demonstrate the generality of our helicity induction approach based on the py–pym unit as *helicity codon*. They suggest the design of various other heterocyclic sequences as structurally instructed units encoding intramolecular self-organization of specific type (helical or not)[6b] like supramolecular self-organization can be programmed and directed through appropriate intermolecular instructions.[3c] As has already been pointed out earlier, [6b] when compared to biopolymers such as proteins, the (py–pym) sequences, the bends, and the helical structures of the polyheterocyclic strands find analogy in the aminoacid sequences, the β-turns, and the α-helix features respectively; in addition, the organisational process itself corresponds to the protein-folding phenomenon. One may also envisage the formation of helical polymers based on appropriate heterocyclic strands; such spring-type polymers can be expected to have interesting physical and mechanical properties.

Experimental Section

General methods: Melting points were measured on a digital Electrotherma apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Bruker AC200 and AM400 spectrometers in $CDCl_3$ at 200 and 400 MHz, respectively, in the concentration range $2-8\times10^{-3}$ M; chemical shifts are given in ppm using a residual solvent proton peak as reference. ^{13}C NMR spectra were recorded on a Bruker AC200 spectrometer in $CDCl_3$ at 50 MHz; chemical shifts are given in ppm using solvent peak as reference. Electronic absorption spectra were measured on a Cary 219 spectrometer in dichloromethane. Fluorescence emission spectra were recorded on an SLM Aminco Series 2 spectrophotometer in dichloromethane. Fast atom bombardment (FAB) mass spectra were recorded at the Service Central d′Analyse du CNRS, Solaise. The microanalyses were carried out at the Service Central de Microanalyse du CNRS, Faculté de Chimie, Strasbourg. THF was distilled over benzophenone/Na. DMSO was distilled over CaH_2. Column chromatography was carried out on Merck alumina activity II-III. Compounds **7**–**12** were prepared according to the procedures described in the literature.[6]

0947-6539/99/0512-3478 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 12

Compound 13: To a refluxing solution of **10**[6b] (1.2 g, 2.07 mmol), **9** (1.8 g, 3.11 mmol),[6b] and [18]crown-6 (0.82 g, 3.12 mmol) in dry THF (90 mL), a solution of *t*BuOK (0.35 g, 3.12 mmol) in dry THF (50 mL) was added dropwise under argon over a period of 60 min and the reaction was refluxed for an additional 30 min. After cooling, acetic acid (30 mL) and NH_4OAc (15 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (400 mL), extracted with chloroform (2 × 250 mL), washed with saturated aqueous $NaHCO_3$ (300 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina eluted with chloroform to afford the ethylvinylether corresponding to **13** as a colorless powder (1.36 g, 62%). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.66$ (t, $^3J = 7.0$ Hz, 3H), 1.14–1.27 (m, 12H), 1.78–2.03 (m, 8H), 3.15–3.30 (m, 8H), 3.98 (d, $^2J = 2.1$ Hz, 1H), 5.25 (d, $^2J = 2.1$ Hz, 1H), 6.63 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 1H), 6.90 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.9$ Hz, 1H), 7.92 (d, $^4J = 1.8$ Hz, 1H), 7.93 (d, $^4J = 1.8$ Hz, 1H), 8.11 (br. d, $^3J = 7.6$ Hz, 1H), 8.11 (d, $^4J = 1.8$ Hz, 1H), 8.12 (d, $^4J = 1.8$ Hz, 1H), 8.23 (d, $^4J = 1.8$ Hz, 1H), 8.28 (d, $^4J = 1.8$ Hz, 1H), 8.36 (d, $^5J = 1.2$ Hz, 1H), 8.44 (br. d, $^3J = 4.9$ Hz, 1H) 8.46 (d, $^4J = 1.8$ Hz, 1H), 8.58 (d, $^4J = 1.8$ Hz, 1H), 8.98 (d, $^5J = 1.2$ Hz, 1H), 9.00 (d, $^5J = 1.2$ Hz, 1H), 9.11 (d, $^5J = 1.2$ Hz, 1H), 9.46 (d, $^5J = 1.2$ Hz, 1H), 9.50 (d, $^5J = 1.2$ Hz, 1H), 9.68 (d, $^5J = 1.2$ Hz, 1H), 10.27 (d, $^5J = 1.2$ Hz, 1H).

A mixture of the vinylether thus obtained (1.36 g, 1.28 mmol), chloroform (5 mL), acetone (200 mL), and hydrochloric acid (2N, 20 mL) was refluxed for 60 min. The reaction was cooled to room temperature and the precipitate which formed was collected by filtration. The solid was washed with acetone, dissolved in chloroform (200 mL), washed with saturated aqueous $NaHCO_3$ (100 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to reprecipitation from dichloromethane/acetone to afford **13** as a colorless powder (1.23 g, 93%). M.p. 197-198.5 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.13–1.24$ (m, 12H), 1.78–1.97 (m, 8H), 2.25 (s, 3H), 3.12–3.28 (m, 8H), 6.61 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 1H), 6.87 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.9$ Hz, 1H), 7.86 (d, $^4J = 1.8$ Hz, 1H), 7.87 (d, $^4J = 1.8$ Hz, 1H), 8.04 (br. d, $^3J = 7.6$ Hz, 1H), 8.08 (d, $^4J = 1.8$ Hz, 1H), 8.12 (br. s, 2H), 8.20 (d, $^5J = 1.2$ Hz, 1H), 8.40 (br. d, $^3J = 4.9$ Hz, 1H) 8.42 (d, $^4J = 1.8$ Hz, 1H), 8.57 (br. s, 2H), 8.92 (d, $^5J = 1.2$ Hz, 1H), 8.98 (d, $^5J = 1.2$ Hz, 1H), 9.19 (d, $^5J = 1.2$ Hz, 1H), 9.44 (d, $^5J = 1.2$ Hz, 1H), 9.45 (d, $^5J = 1.2$ Hz, 1H), 9.56 (d, $^5J = 1.2$ Hz, 1H), 10.18 (d, $^5J = 1.2$ Hz, 1H); MS (FAB): *m/z* (%): 1038.2 (100) [MH$^+$]; $C_{55}H_{51}N_{13}OS_4$ (1037.32): calcd C 63.63, H 4.95, N 17.55; found C 64.40, H 5.20, N 17.67.

Compound 14: To a refluxing solution of **13** (622 mg, 0.6 mmol), **8** (581 mg, 1.2 mmol), [6b] and [18]crown-6 (238 mg, 0.9 mmol) in dry THF (30 mL) a solution of *t*BuOK (101 mg, 0.9 mmol) in dry THF (45 mL) was added dropwise under argon over a period of 2 h and the reaction was refluxed for an additional 1 h. After cooling, acetic acid (12 mL) and NH_4OAc (6 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (300 mL), extracted with chloroform (2 × 200 mL), washed with saturated aqueous $NaHCO_3$ (200 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina; elution with chloroform followed by reprecipitation from dichloromethane/acetone afforded **14** as a yellow powder (435 mg, 51%). M.p. 218-220 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.97$ (t, $^3J = 7.3$ Hz, 3H), 1.07–1.21 (m, 18H), 1.40–1.93 (m, 14H), 2.77–3.17 (m, 14H), 6.29 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 1H), 6.45 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.9$ Hz, 1H), 6.79 (s, 1H), 7.53 (d, $^4J = 1.8$ Hz, 1H), 7.68–7.71 (m, 3H), 7.72 (br. d, $^3J = 7.6$ Hz, 1H), 7.74 (d, $^4J = 1.8$ Hz, 1H), 7.77 (d, $^4J = 1.8$ Hz, 1H), 7.82 (d, $^4J = 1.8$ Hz, 1H), 7.86–7.89 (m, 3H), 8.09 (br. d, $^3J = 4.9$ Hz, 1H), 8.37 (d, $^5J = 1.2$ Hz, 1H), 8.75 (d, $^5J = 1.2$ Hz, 1H), 8.83 (d, $^5J = 1.2$ Hz, 1H), 8.87 (br. s, 2H), 8.89 (d, $^5J = 1.2$ Hz, 1H), 8.93 (d, $^5J = 1.2$ Hz, 1H), 9.02 (d, $^5J = 1.2$ Hz, 1H), 9.29 (d, $^5J = 1.2$ Hz, 1H), 9.41(d, $^5J = 1.2$ Hz, 1H); MS (FAB): *m/z* (%): 1427.1 (100) [MH$^+$]; $C_{74}H_{74}N_{16}OS_7$ (1426.43): calcd C 62.25, H 5.23, N 15.71; found C 62.18, H 5.25, N 15.58.

Compound 15: To a refluxing solution of **13** (0.26 g, 0.25 mmol), **9** (0.23 g, 0.4 mmol),[6b] and [18]crown-6 (0.10 g, 0.38 mmol) in dry THF (10 mL) a solution of *t*BuOK (0.04 g, 0.38 mmol) in dry THF (20 mL) was added dropwise under argon over a period of 40 min. After cooling, acetic acid (5 mL) and NH_4OAc (2.5 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (100 mL), extracted with chloroform (2 × 100 mL), washed with saturated aqueous $NaHCO_3$ (50 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina and eluted with chloroform to afford the ethylvinylether corresponding to **15** as a colorless powder (0.10 g, 27%). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.35$ (t, $^3J = 7.0$ Hz, 3H), 1.13–1.32 (m, 18H), 1.77–2.02 (m, 12H), 3.11–3.31 (m, 14H), 3.76 (d, $^2J = 2.1$ Hz, 1H), 4.99 (d, $^2J = 2.1$ Hz, 1H), 6.24 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 1H), 6.68 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.9$ Hz, 1H), 7.61 (d, $^4J = 1.8$ Hz, 1H), 7.67 (d, $^4J = 1.8$ Hz, 1H), 7.76 (br. d, $^3J = 7.6$ Hz, 1H), 7.79 (d, $^4J = 1.8$ Hz, 1H), 7.89 (d, $^4J = 1.8$ Hz, 1H), 7.96–9.98 (m, 3H), 8.00 (br.s, 2H), 8.07 (d, $^4J = 1.8$ Hz, 1H), 8.13 (d, $^4J = 1.8$ Hz, 1H), 8.17 (d, $^4J = 1.8$ Hz, 1H), 8.18 (d, $^4J = 1.8$ Hz, 1H), 8.29 (br. d, $^3J = 4.9$ Hz, 1H) 8.69 (d, $^5J = 1.2$ Hz, 1H), 8.79 (d, $^5J = 1.2$ Hz, 1H), 9.10 (d, $^5J = 1.2$ Hz, 1H), 9.14 (d, $^5J = 1.2$ Hz, 1H), 9.20 (d, $^5J = 1.2$ Hz, 1H), 9.21 (d, $^5J = 1.2$ Hz, 1H), 9.30 (d, $^5J = 1.2$ Hz, 1H), 9.35 (d, $^5J = 1.2$ Hz, 1H), 9.43 (d, $^5J = 1.2$ Hz, 1H), 9.70 (d, $^5J = 1.2$ Hz, 1H), 9.72 (d, $^5J = 1.2$ Hz, 1H).

A mixture of the vinylether thus obtained (102 mg, 0.067 mmol), acetone (200 mL), and hydrochloric acid (2N, 10 mL) was refluxed for 80 min. The reaction was cooled to room temperature and the precipitate which formed was collected by filtration. The solid was washed with acetone, dissolved in chloroform (100 mL), washed with saturated aqueous $NaHCO_3$ (50 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to reprecipitation from chloroform/acetone to afford **15** as a colorless powder (80 mg, 80%). M.p. 255–257 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.11–1.30$ (m, 18H), 1.72–2.03 (m, 12H), 2.01 (s, 3H), 3.17–3.29 (m, 12H), 6.22 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 1H), 6.61 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.9$ Hz, 1H), 7.54 (d, $^4J = 1.8$ Hz, 1H), 7.60 (d, $^4J = 1.8$ Hz, 1H), 7.70 (br. d, $^3J = 7.6$ Hz, 1H), 8.74 (d, $^4J = 1.8$ Hz, 1H), 7.85 (d, $^4J = 1.8$ Hz, 1H), 7.88 (d, $^4J = 1.8$ Hz, 1H), 7.90 (d, $^4J = 1.8$ Hz, 1H), 7.96 (d, $^4J = 1.8$ Hz, 1H), 8.00 (d, $^4J = 1.8$ Hz, 1H), 8.05 (d, $^4J = 1.8$ Hz, 1H), 8.10 (d, $^4J = 1.8$ Hz, 1H), 8.13 (d, $^4J = 1.8$ Hz, 1H), 8.14 (d, $^4J = 1.8$ Hz, 1H), 8.21 (d, $^5J = 1.2$ Hz, 1H), 8.22 (br. d, $^3J = 4.9$ Hz, 1H) 8.59 (d, $^5J = 1.2$ Hz, 1H), 8.98 (d, $^5J = 1.2$ Hz, 1H), 9.08 (d, $^5J = 1.2$ Hz, 1H), 9.10 (d, $^5J = 1.2$ Hz, 1H), 9.16 (d, $^5J = 1.2$ Hz, 1H), 9.17 (d, $^5J = 1.2$ Hz, 1H), 9.20 (d, $^5J = 1.2$ Hz, 1H), 9.30 (br. s, 2H), 9.60 (d, $^5J = 1.2$ Hz, 1H), 9.61 (d, $^5J = 1.2$ Hz, 1H); MS (FAB): *m/z* (%): 1496.4 (100) [MH$^+$]; $C_{79}H_{73}N_{19}OS_6$ (1495.46): calcd C 63.39, H 4.92, N 17.79; found C 64.24, H 4.88, N 17.51.

Compound 16: To a magnetically stirred solution of **7** (4.8 g, 25 mmol)[6b] in dry DMSO (180 mL), NaH (1.32 g, 55 mmol) was added portionwise at room temperature under argon over a period of 30 min and the reaction was stirred for an additional 20 min. To the mixture, carbon disulfide (1.67 mL, 27.5 mmol) was added dropwise under ice-water cooling followed by dropwise addition of propyl iodide (5.31 mL, 55 mmol). The mixture was sirred at room temperarure for 20 h and then poured into water (500 mL) and extracted with dichloromethane (300 + 200 mL). The extracts were combined, washed well with water (3 × 300 mL), and dried with $MgSO_4$. After removal of the solvent, the residue was subjected to chromatography on alumina eluted with dichloromethylene followed by recrystalization from hexane to give **16** as orange crystals (6.0 g, 68%). M.p. 85.5–86.5 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.07$ (t, $^3J = 7.3$ Hz, 3H), 1.11 (t, $^3J = 7.3$ Hz, 3H), 1.43 (t, $^3J = 7.0$ Hz, 3H), 1.68–1.92 (m, 4H), 3.08 (t, $^3J = 7.0$ Hz, 2H), 3.11 (t, $^3J = 7.0$ Hz, 2 Hz), 3.97 (q, $^3J = 7.0$ Hz, 2H), 4.52 (d, $^2J = 2.1$ Hz, 1H), 5.65 (d, $^2J = 2.1$ Hz, 1H), 7.58 (s, 1H), 8.36 (d, $^5J = 1.2$ Hz, 1H), 9.19 (d, $^5J = 1.2$ Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.66$ (2C), 14.50, 20.97, 22.33, 33.65, 36.33, 63.93, 88.26, 108.36, 113.25, 156.80, 157.68, 162.01, 162.42, 170.17, 182.59; MS (FAB): *m/z* (%): 353.2 (100) [MH$^+$]; $C_{17}H_{24}N_2O_2S_2$ (352.13): calcd C 57.93, H 6.87, N 7.95; found C 57.99, H 6.76, N 7.94.

Compound 17: To a magnetically stirred solution of *t*BuOK (2.9 g, 26 mmol) in dry THF (100 mL) a solution of **7** (3.3 g, 17 mmol)[6b] in dry THF (30 mL) was added dropwise at room temperature under argon over a period of 10 min and the reaction was stirred for an additional 20 min. To the mixture, a solution of **16** (6.0 g, 17 mmol) in dry THF (100 mL) was added over a period of 10 min and the mixture was sirred at room temperarure for 17 h. Acetic acid (100 mL) and NH_4OAc (20 g) were then added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (500 mL), extracted with chloroform (500 mL), washed with saturated aqueous $NaHCO_3$ (300 mL), and dried with $MgSO_4$. After removal of the solvent, the residue was subjected to chromatography on alumina eluted with chloroform to afford the bis(vinylether) which was hydrolyzed in a mixture of acetone (120 mL) and hydrochloric acid (2N, 20 mL). After refluxing for 30 min, the reaction was cooled, poured into saturated aqueous $NaHCO_3$ (300 mL), extracted with chloroform (300 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina; elution with

chloroform followed by reprecipitation from chloroform/acetone produced **17** as a colorless powder (2.37 g, 36%). M.p. 203.5-204.5 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.14$ (t, $^3J = 7.0$ Hz, 3H), 1.85 (m, 2H), 2.80 (s, 6H), 3.16 (t, $^3J = 7.0$ Hz, 2H), 8.43 (s, 2H), 8.94 (d, $^5J = 1.2$ Hz, 2H), 9.41 (d, $^5J = 1.2$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.59$, 21.89, 25.90, 32.99, 114.11, 120.24, 153.14, 153.51, 158.69, 160.38, 164.42, 199.12; MS (FAB): *m/z* (%): 394.0 (100) [MH$^+$]; $C_{20}H_{19}N_5O_2S$ (393.13): calcd C 61.05, H 4.87, N 17.81; found C 61.28, H 5.02, N 17.82.

Compound 18: To a refluxing solution of **17** (0.30 g, 0.76 mmol), **9** (2.21 g, 3.8 mmol),[6b] and [18]crown-6 (0.60 g, 2.3 mmol) in dry THF (30 mL), a solution of *t*BuOK (0.26 g, 2.3 mmol) in dry THF (30 mL) was added dropwise under argon over a period of 2 h. After cooling, acetic acid (15 mL) and NH_4OAc (8 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (200 mL), extracted with chloroform (2×200 mL), washed with saturated aqueous $NaHCO_3$ (100 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on alumina eluted with chloroform to afford the bis(ethylvinylether) which was hydrolyzed in a mixture of chloroform (1 mL), acetone (50 mL), and hydrochloric acid (2 N, 20 mL). After refluxing 40 min, the reaction was cooled to room temperature and the precipitate which formed was collected by filtration. The solid was washed with acetone, dissolved in chloroform (200 mL), washed with saturated aqueous $NaHCO_3$ (100 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was subjected to reprecipitation from chloroform/acetone to afford **18** as a colorless powder (0.29 g, 25%). M.p. 230–232 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.16$–1.26 (m, 15H), 1.78–1.99 (m, 10H), 2.12 (s, 6H), 3.15–3.26 (m, 10H), 7.93 (d, $^4J = 1.8$ Hz, 2H), 7.97 (d, $^4J = 1.8$ Hz, 2H), 8.09 (s, 2H), 8.12 (d, $^4J = 1.8$ Hz, 2H), 8.16 (d, $^4J = 1.8$ Hz, 2H), 8.41 (d, $^5J = 1.2$ Hz, 2H), 9.03 (d, $^5J = 1.2$ Hz, 2H), 9.10 (d, $^5J = 1.2$ Hz, 2H), 9.19 (d, $^5J = 1.2$ Hz, 2H), 9.38 (d, $^5J = 1.2$ Hz, 2H), 9.74 (d, $^5J = 1.2$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.84$, 21.78(m), 25.02, 32.73, 33.10, 33.18, 113.26, 114.44, 114.51, 118.09, 118.30, 118.63, 119.29, 119.55, 151.37, 151.96, 152.37, 152.66, 152.77, 152.84, 153.36, 158.17, 158.19, 158.30, 158.32, 158.39, 162.11, 162.47, 162.81, 162.88, 163.39, 196.91; MS (FAB): *m/z* (%): 1310.3 (100) [MH$^+$]; $C_{68}H_{63}N_{17}O_2S_5$ (1309.40): calcd C 62.32, H 4.85, N 18.18; found C 62.41, H 4.98, N 18.20.

Compound 1: To a refluxing solution of **18** (301 mg, 0.23 mmol), **11** (587 mg, 1.15 mmol),[6b] and [18]crown-6 (243 mg, 0.92 mmol) in dry THF (20 mL), a solution of *t*BuOK (103 mg, 0.92 mmol) in dry THF (20 mL) was added dropwise under argon over a period of 2 h. After cooling, acetic acid (4 mL) and NH_4OAc (2 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (150 mL), extracted with chloroform (3×100 mL), washed with saturated aqueous $NaHCO_3$ (100 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was chromatographed on alumina. Elution with chloroform gave crude **1**, which was further purified by preparative TLC (alumina, chloroform) and reprecipitation from chloroform/acetone to afford **1** as a colorless powder (165 mg, 34%). M.p. 287–289 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.11$ (t, $^3J = 7.0$ Hz, 6H), 1.17 (t, $^3J = 7.0$ Hz, 6H), 1.24 (t, $^3J = 7.0$ Hz, 6H), 1.35 (t, $^3J = 7.0$ Hz, 6H), 1.41 (t, $^3J = 7.0$ Hz, 3H), 1.71–2.20 (m, 18H), 3.06–3.43 (m, 18H), 6.03 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 2H), 6.55 (ddd, $^3J = 7.6$ Hz, $^3J = 4.7$ Hz, $^4J = 1.0$ Hz, 2H), 7.35 (d, $^4J = 1.8$ Hz, 2H), 7.44 (d, $^4J = 1.8$ Hz, 2H), 7.49 (d, $^4J = 1.8$ Hz, 2H), 7.50 (br. d, $^3J = 7.6$ Hz, 2H), 7.56 (d, $^4J = 1.8$ Hz, 2H), 7.67 (d, $^4J = 1.8$ Hz, 2H), 7.78 (d, $^4J = 1.8$ Hz, 2H), 7.86 (d, $^4J = 1.8$ Hz, 2H), 7.93 (d, $^4J = 1.8$ Hz, 2H), 7.99 (d, $^4J = 1.8$ Hz, 2H), 8.18 (br. d, $^3J = 4.7$ Hz, 2H), 8.52 (d, $^5J = 1.2$ Hz, 2H), 8.92 (d, $^5J = 1.2$ Hz, 2H), 8.93 (d, $^5J = 1.2$ Hz, 2H), 8.94 (d, $^5J = 1.2$ Hz, 2H), 9.03 (d, $^5J = 1.2$ Hz, 2H), 9.04 (d, $^5J = 1.2$ Hz, 2H), 9.13 (d, $^5J = 1.2$ Hz, 2H), 9.33 (d, $^5J = 1.2$ Hz, 2H); UV/Vis (CH_2Cl_2): λ_{max} (ε) = 289 nm (203000); MS (FAB): *m/z* (%): 2145.5 (25) [MH$^+ + 5$], 2144.5 (48) [MH$^+ + 4$], 2143.5 (75) [MH$^+ + 3$], 2142.5 (100) [MH$^+ + 2$], 2141.5 (100) [MH$^+ + 1$], 2140.5 (77) [MH$^+$]; $C_{114}H_{105}N_{27}S_9$ (2139.65).

Compound 2: To a refluxing solution of **15** (50 mg, 0.033 mmol), **12** (65 mg, 0.067 mmol),[6b] and [18]crown-6 (14 mg, 0.050 mmol) in dry THF (2 mL), a solution of *t*BuOK (6 mg, 0.050 mmol) in dry THF (2 mL) was added dropwise under argon over a period of 2 h. After cooling, acetic acid (1 mL) and NH_4OAc (0.5 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (20 mL), extracted with chloroform (3×30 mL), washed with saturated aqueous $NaHCO_3$ (40 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was chromatographed on alumina. Elution with chloroform gave crude **2**, which was further purified by preparative TLC (alumina, chloroform) and reprecipitation from chloroform/acetone to afford **2** as a colorless powder (5.2 mg, 7%). M.p. > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (t, $^3J = 7.0$ Hz, 6H), 1.14 (t, $^3J = 7.0$ Hz, 6H), 1.24 (t, $^3J = 7.0$ Hz, 6H), 1.35 (t, $^3J = 7.0$ Hz, 6H), 1.38 (t, $^3J = 7.0$ Hz, 6H), 1.70–2.14 (m, 20H), 3.04–3.34 (m, 20H), 6.01 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 2H), 6.55 (br. dd, $^3J = 7.6$ Hz, $^3J = 4.7$ Hz, 2H), 7.32 (d, $^4J = 1.8$ Hz, 2H), 7.35 (d, $^4J = 1.8$ Hz, 2H), 7.40 (d, $^4J = 1.8$ Hz, 2H), 7.45 (br. d, $^3J = 7.6$ Hz, 2H), 7.47 (d, $^4J = 1.8$ Hz, 2H), 7.48 (d, $^4J = 1.8$ Hz, 2H), 7.61 (d, $^4J = 1.8$ Hz, 2H), 7.73 (d, $^4J = 1.8$ Hz, 2H), 7.83 (d, $^4J = 1.8$ Hz, 2H), 7.86 (d, $^4J = 1.8$ Hz, 2H), 7.98 (d, $^4J = 1.8$ Hz, 2H), 8.18 (br. d, $^3J = 4.7$ Hz, 2H), 8.56 (d, $^5J = 1.2$ Hz, 2H), 8.743 (d, $^5J = 1.2$ Hz, 2H), 8.86 (s, 4H), 8.90 (d, $^5J = 1.2$ Hz, 1H), 8.91 (d, $^5J = 1.2$ Hz, 2H), 8.94 (d, $^5J = 1.2$ Hz, 2H), 9.00 (d, $^5J = 1.2$ Hz, 2H), 9.05 (d, $^5J = 1.2$ Hz, 1H), 9.26 (d, $^5J = 1.2$ Hz, 2H); MS (FAB): *m/z* (%): 2374.7 (33) [MH$^+ + 5$], 2373.7 (56) [MH$^+ + 4$], 2372.7 (84) [MH$^+ + 3$], 2371.7 (100) [MH$^+ + 2$], 2370.7 (970) [MH$^+ + 1$], 2369.7 (67) [MH$^+$]; $C_{126}H_{116}N_{30}S_{10}$ (2368.72).

Compound 3: To a refluxing solution of **18** (142 mg, 0.11 mmol), **12** (525 mg, 0.54 mmol),[6b] and [18]crown-6 (114 mg, 0.43 mmol) in dry THF (10 mL), a solution of *t*BuOK (48 mg, 0.43 mmol) in dry THF (10 mL) was added dropwise under argon over a period of 90 min. After cooling, acetic acid (2 mL) and NH_4OAc (1 g) were added to the reaction. The mixture was refluxed for 90 min, cooled, poured into water (100 mL), extracted with chloroform (3×70 mL), washed with saturated aqueous $NaHCO_3$ (70 mL), and dried with Na_2SO_4. After removal of the solvent, the residue was chromatographed on alumina. Elution with chloroform gave crude **3**, which was further purified by preparative TLC (alumina, chloroform) and reprecipitation from chloroform/acetone to afford **3** as a colorless powder (18 mg, 5%). M.p. > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.07$ (t, $^3J = 7.0$ Hz, 6H), 1.11 (t, $^3J = 7.0$ Hz, 6H), 1.19 (t, $^3J = 7.0$ Hz, 6H), 1.31 (t, $^3J = 7.0$ Hz, 6H), 1.33 (t, $^3J = 7.0$ Hz, 3H), 1.34 (t, $^3J = 7.0$ Hz, 12H), 1.68–2.07 (m, 26H), 3.00–3.27 (m, 26H), 5.90 (td, $^3J = 7.6$ Hz, $^4J = 1.8$ Hz, 2H), 6.48 (ddd, $^3J = 7.6$ Hz, $^3J = 4.7$ Hz, $^4J = 1.0$ Hz, 2H), 7.12 (s, 2H), 7.19 (d, $^4J = 1.8$ Hz, 2H), 7.20 (d, $^4J = 1.8$ Hz, 2H), 7.25 (d, $^4J = 1.8$ Hz, 2H), 7.29 (d, $^4J = 1.8$ Hz, 2H), 7.33 (br. d, $^3J = 7.6$ Hz, 2H), 7.36 (d, $^4J = 1.8$ Hz, 2H), 7.56 (d, $^4J = 1.8$ Hz, 2H), 7.64 (d, $^4J = 1.8$ Hz, 2H), 7.77 (d, $^4J = 1.8$ Hz, 2H), 7.78 (d, $^4J = 1.8$ Hz, 2H), 7.86 (d, $^4J = 1.8$ Hz, 2H), 8.12 (br. d, $^4J = 4.7$ Hz, 2H), 8.45 (d, $^4J = 1.2$ Hz, 2H), 8.52 (d, $^5J = 1.2$ Hz, 2H), 8.55 (d, $^5J = 1.2$ Hz, 2H), 8.65 (d, $^5J = 1.2$ Hz, 2H), 8.66 (d, $^5J = 1.2$ Hz, 2H), 8.67 (d, $^5J = 1.2$ Hz, 2H), 8.72 (d, $^5J = 1.2$ Hz, 4H), 8.73 (d, $^5J = 1.2$ Hz, 2H), 8.80 (d, $^5J = 1.2$ Hz, 2H), 8.90

Table 2. Crystallographic data for compound **1**.

formula	$C_{114}H_{105}N_{27}S_9 \cdot CHCl_3$
M_r[g mol^{-1}]	3
T(K)	200(1)
wavelength [Å]	0.71073
crystal system	monoclinic
space group	$P2_1$
a [Å]	15.565(3)
b [Å]	24.386(5)
c [Å]	15.634(8)
α [°]	90
β [°]	109.24(5)
γ [°]	90
volume [Å]	5603(3)
Z	2
ρ_{cald} [g cm^{-3}]	1.340
$\mu(Mo_{K\alpha})$ [mm^{-1}]	0.312
F(000)	2360
crystal size [mm]	$0.20 \times 0.20 \times 0.10$
Φ [°]	2.17 – 26.02
index ranges	$-19 \le h \le 14$, $-26 \le k \le 27$, $-19 \le l \le 19$
reflections collected	29897
R(int)	0.0488
independent reflections	19611
data/restraints/parameters	19611/35/1394
GoF S	1.034
final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0633$, $wR_2 = 0.1613$
R indices (all data)	$R_1 = 0.0825$, $wR_2 = 0.1765$
largest diff. peak/hole [e Å^{-3}]	0.521/ – 0.365
absolute structure parameter	0.32(6)

0947-6539/99/0512-3480 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 12

(d, $^5J = 1.2$ Hz, 2H), 9.07 (d, $^5J = 1.2$ Hz, 2H); UV/Vis (CH_2Cl_2): λ_{max} (ε) = 289 nm (251000); MS (FAB): *m/z* (%): 3062.1 (53) [MH$^+ + 5$], 3061.1 (75) [MH$^+ + 4$], 3060.1 (95) [MH$^+ + 3$], 3059.1 (100) [MH$^+ + 2$], 3058.1 (85) [MH$^+ + 1$], 3057.1 (54) [MH$^+$]; $C_{162}H_{149}N_{39}S_{13}$ (355.92).

X-Ray structure determination of 1: The measurements were carried out on a STOE-IPDS diffractometer ($Mo_{K\alpha}$ radiation with graphite monochromator) at $T = 200$ K. Table 2 summarizes the crystal data, data collection and refinement parameters. All calculations were performed with the SHELX-97 package.[13] The structures were solved by direct methods and were refined by full-matrix least-squares techniques based on F^2. All hydrogen atoms, the disordered SPr groups, and solvent molecules were refined isotropically. The hydrogen atoms were placed in calculated positions with $U(H) = 1.5\,U_{eq}(C)$ for methyl groups and $U(H) = 1.2\,U_{eq}(C)$ for others. Molecular graphics were performed with SCHAKAL97.[14] Crystallographic data (excluding structure factors) for the structure of compound **1** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-135177. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK (fax: (+44) 1223-336-033; e-mail: deposit @ccdc.cam.ac.uk).

Acknowledgment

We thank Dr. Patrick Maltèse and Roland Graff for the NMR measurements. M. O. is grateful to Université Louis Pasteur, Strasbourg, and the Ministry of Education, Science, Sports, and Culture of Japan for financial support.

[1] J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, **1995**.
[2] C. Bränden, J. Tooze, *Introduction to Protein Structure*, Garland, New York, **1991**.
[3] a) A. E. Rowan, R. J. M. Nolte, *Angew. Chem.* **1998**, *110*, 65; *Angew. Chem. Int. Ed.* **1998**, *37*, 63; b) C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005; c) see ref. [1], Ch. 9.
[4] For recent examples, see: a) D. B. Amabilino, E. Ramos, J.-L. Serrano, J. Veciana, *Adv. Mater.* **1998**, *10*, 1001; b) J. J. L. M. Cornelissen, M. Fischer, N. A. J. M. Sommerdijk, R. J. M. Nolte, *Science* **1998**, *280*, 1427; c) C. A. Slate, D. R. Striplin, J. A. Moss, P. Chen, B. W. Erickson, T. J. Meyer, *J. Am. Chem. Soc.* **1998**, *120*, 4885; d) J. C. Nelson, J. G. Saven, J. S. Moore, P. G. Wolynes, *Science* **1997**, *277*, 1793; e) Y. Hamuro, S. J. Geib, A. D. Hamilton, *J. Am. Chem. Soc.* **1997**, *119*, 10587; f) A. Tanatani, H. Kagechika, I. Azumaya, R. Fukutomi, Y. Ito, K. Yamaguchi and K. Shudo, *Tetrahedron Lett.* **1997**, *38*, 4425; g) M. Kauranen, T. Verbiest, C. Boutton, M. N. Teerenstra, K. Clays, A. J. Schouten, R. J. M. Nolte, A. Persoons, *Science* **1995**, *270*, 966; h) R. S. Lokey and B. L. Iverson, *Nature* **1995**, *375*, 303; i) D. J. Williams, H. M. Colquhoun, C. A. O'Mahoney, *J. Chem. Soc. Chem. Commun.* **1994**, 1643; j) C. Y. Cho, E. J. Moran, S. R. Cherry, J. C. Stephans, S. P. A. Fodor, C. L. Adams, A. Sundaram, J. W. Jacobs, P. G. Schultz, *Science* **1993**, *261*, 1303; k) J. S. Nowick, N. A. Powell, E. J. Martinez, E. M. Smith, G. Noronha, *J. Org. Chem.* **1992**, *57*, 3763; l) M. Hagihara, N. J. Anthony, T. J. Stout, J. Clargy, S. L. Schreiber, *J. Am. Chem. Soc.* **1992**, *114*, 6568; m) D. Philp, J. F. Stoddart, *Syn. Lett.* **1991**, 445.
[5] a) G. S. Hanan, J.-M. Lehn, N. Krytsakas, J. Fisher, *J. Chem. Soc. Chem. Commun.* **1995**, 765; b) G. S. Hanan, U. S. Schubert, D. Volkmer, E. Rivière, J.-M. Lehn, N. Krytsakas, J. Fisher, *Can. J. Chem.* **1997**, *75*, 169.
[6] a) D. M. Bassani, J.-M. Lehn, G. Baum, D. Fenske, *Angew. Chem.* **1997**, *109*, 1931; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1845; b) D. M. Bassani, J.-M. Lehn, *Bull. Soc. Chim. Fr.* **1997**, *134*, 897.
[7] a) G. S. Hanan, C. R. Arana, J.-M. Lehn, D. Fenske, *Angew. Chem.* **1995**, *107*, 1191; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1122; b) G. S. Hanan, C. R. Arana, J.-M. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **1996**, *2*, 1292; b) G. S. Hanan, C. R. Arana, J.-M. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **1996**, *2*, 1292; c) G. S. Hanan, D. Volkmer, U. S. Schubert, J.-M. Lehn, G. Baum, D. Fenske, *Angew. Chem.* **1997**, *109*, 1929; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1842; d) D. M. Bassani, J.-M. Lehn, K. Fromm, D. Fenske, *Angew. Chem.* **1998**, *110*, 2534; *Angew. Chem. Int. Ed.* **1998**, *37*, 2364.
[8] K. T. Potts, *Bull. Soc. Chem. Belg.* **1990**, *99*, 741.
[9] C. R. Cantor, P. R. Schimmel, *Biophysical Chemistry*, Freeman, New York, **1980**.
[10] C. L. Cheng, D. S. N. Murthy, G. L. Retchie, *J. Chem. Soc. Faraday Trans. 2* **1972**, *68*, 1679.
[11] T. Yamamoto, T. Maruyama, T. Ikeda, M. Sisido, *J. Chem. Soc. Chem. Commun.* **1990**, 1306.
[12] S. T. Howard, *J. Am. Chem. Soc.* **1996**, *118*, 10269.
[13] G. M. Sheldrick, SHELX-97, Universität Göttingen, **1997**.
[14] E. Keller, SCHAKAL97, Universität Freiburg, **1997**.

Received: April 15, 1999 [F 1725]