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Intramolecular hydrogen bonding in acylated 2,2′-bipyridine-3,3′-diamines

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Abstract. Various di- and monoacylated 2,2′-bipyridine-3,3′-diamines (amides **1a-f, 8, 9**, ureas **1g-h, 8b** and acylureas **1i-j**) have been synthesized and characterized. All molecules show strong intramolecular hydrogen bonding between the acyl NH of one ring and the pyridine N-1 of the other (and *vice versa*), as is deduced from the low field ^{1}H NMR resonances of the acyl NH protons, which range from δ 12.6 to 15.0 ppm in $CDCl_3$. The nature of the secondary structure of the (di)acylated 2,2′-bipyridine-3,3′-diamines has been investigated using a variety of techniques including variable-temperature ^{1}H NMR and CD spectroscopy.

Introduction

The study of intra- and intermolecular hydrogen bonding has always been a central theme within chemistry. Recently, interest in supramolecular architectures has stimulated further research in the area of secondary interactions, in which hydrophobic interactions[1], ligand formation with metal ions[2] and hydrogen bonding[3] are important instruments to obtain well-defined secondary and tertiary structures in complex molecules, as exemplified by models for α-helices in peptides or by the metal ion induced self-assembly of 2,6-oligopyridines[4]. These principles may also lead to supramolecular architectures such as coiled coils[1b], the self-assembly of double helical metal complexes[2b] and the aggregates formed by trivalent melamine derivatives and trivalent isocyanurates[3]. Cooperativity is an important feature in these systems. A recent example of the cooperativity of hydrogen bonding in monomolecular systems is observed in oligo(2-aminobenzamides)[5] whose helical secondary structure can only exist due to the presence of a number of hydrogen bonds. In the late seventies, *Kaczmarek* and coworkers synthesized 2,2′-bipyridin-3,3′-diamines and derivatives thereof in a search for new biologically active compounds[6a-c]. A number of them, *e.g.* 3,3′-bis(acetylamino)-2,2′-bipyridine (**1**, R = CH_3), should have the possibility to exhibit strong intramolecular hydrogen bonding (Figure 1). However, no reports on this phenomenon have been made. This contrasts with the extensive use of the 2,2′-bipyridine moiety as a ligand for metals in supramolecular architectures. No examples are known that have taken advantage of the hydrogen bonding capacities of acylated 2,2′-bipyridine-3,3′-diamines in supramolecular chemistry.
In this paper, we report on the synthesis and characterization of a number of new derivatives of 2,2′-bipyridine-3,3′-diamines and their strong intramolecular hydrogen bonding using NMR and CD spectroscopy; the topic of cooperativity is also discussed.

Results and discussion

1. Synthesis

Diacylated 2,2′-bipyridine-3,3′-diamines **1a-j** (Table I) were synthesized from key precursor 2,2′-bipyridine-3,3′-diamine (**3**). The latter was easily obtained by the Ullmann coupling of 2-chloro-3-nitropyridine, furnishing **2**, followed by electron transfer reduction of the nitro groups (Scheme 1), in an overall yield of 54%[6a,7]. Three classes of diacylated 2,2′-bipyridine-3,3′-diamines were synthesized: diamides, diureas, and bis(acylureas). The diamide (entries 2–7) and the diurea derivatives (entries 8–9) were obtained by reaction of diamine **3** with the corresponding acid chlorides or isocyanates, respectively, which were commercially available or easily accessible through literature procedures[8–10]. Synthesis and purification were straightforward and yields satisfactory. Bis(acylurea) derivatives were obtained from diamine **3** and the corresponding acyl isocyanates. Benzoyl isocyanate, obtained by treatment of benzamide with oxalyl chloride[8], and **3** gave rise to benzoylurea derivative **1i** (entry 10). However,

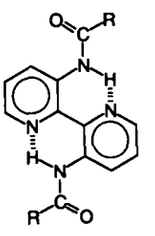

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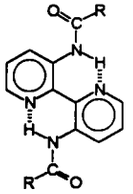
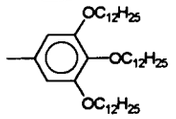
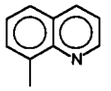
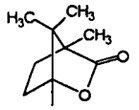
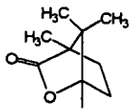
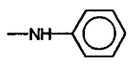
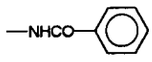
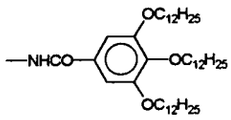
Figure 1. Diacylated 2,2′-bipyridine-3,3′-diamines.

Table I Diacylated 3,3'-diamines-2,2'-bipyridines: relevant ^{1}H-NMR data [a]

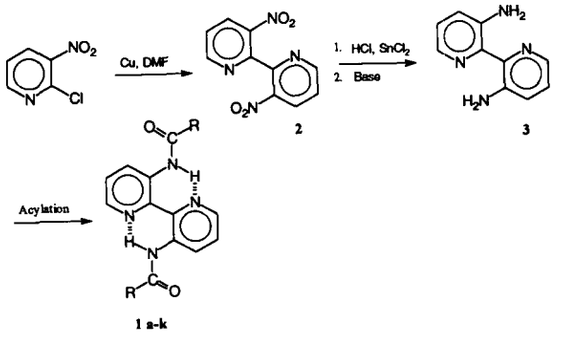
Entry	Compound	Yield (%)	δ (N-H)	δ (H-4)	δ (H-6)
1	3	56	6.26	7.02	7.96
	 R =				
2	**1a** —n-C_5H_{12}	73	13.12	9.06	8.25
3	**1b** 	62	14.59	9.42	8.41
4	**1c** 	72	14.11	9.35	8.38
5	**1d** 	38	13.74	9.31	8.35
6	**1e** 	68	14.97	9.22	8.58
7	**1f** 	70	14.97	9.22	8.58
8	**1g** —NH— 	80	11.30; 9.65[b]	8.72[b]	8.39[b]
9	**1h** —NH-n-C_4H_9	34	12.57; 4.63	8.86	8.10
10	**1i** —NHCO— 	70	10.18[c]	9.23[c]	8.96[c]
11	**1j** —NHCO— 	57	13.28; 8.29	8.79	8.69

[a] All δ values are expressed in ppm and were measured in $CDCl_3$ unless otherwise specified. [b] DMSO-d6. [c] $CDCl_3$/trifluoroacetic acid 3/1.

this bis(acylurea) derivative proved to be insoluble in all common organic solvents. Therefore, to enhance solubility, a derivative with long alkoxy chains, **1j** (entry 11), was prepared in three steps starting from 3,4,5-tris(dodecyloxy)benzoyl chloride[10].

Model compounds **7a-c**, being "monomeric" counterparts of **1b, d,** and **f**, respectively, (Table II) were synthesized to study the specific effect of intramolecular hydrogen bonding on the bipyridine system. The amides were obtained by treating pyridin-3-amine with the corresponding acid chloride (entries 12–14).

In order to determine whether cooperativity is operative in the diacetylated 2,2'-bipyridine-3,3'-diamines, monofunctionalized bipyridines **8a** and **8b** were synthesized as well (Table III). The former compound was obtained from a two step procedure via the symmetrical dipyrido[5,4-*b*:6,7-*b*][1,3]diazepinium intermediate[6c]. In the latter case, however, we discovered that the reaction of **3** with 2 equivalents of *(R)*-α-methylbenzyl isocyanate afforded the monoacylated product **8b** only, as a consequence of precipitation. A survey of the monoacylated compounds (entries 15–16) and the yields obtained are given in Table III. Reaction of compounds **8a-b** with benzene-1,4-dicarbonyl dichloride gave rise to oligomers **9a-b** (Figure 2). Oligomer



Scheme 1. Synthesis of N,N'-diacylated 2,2-bipyridine-3,3'-diamines.

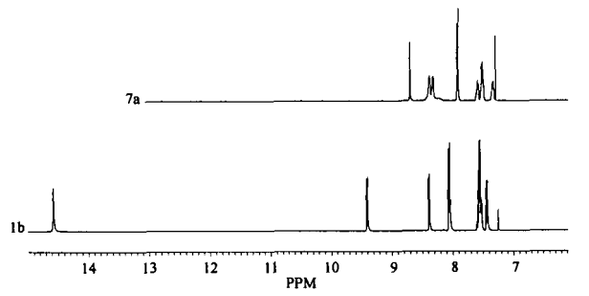


Figure 3. Comparison of 3,3'-bis(benzoylamino)-2,2'-bipyridine (**1b**) *with its monomeric counterpart* **7a**.

9a is insoluble in organic solvents while oligomer **9b** can only be dissolved in polar aprotic solvents such as DMSO and DMF at elevated temperatures.

2. ^1H NMR spectroscopy

In Table I the relevant ^1H NMR data of diacylated compounds **1a-j** (entries 2–11) are summarized and compared to the data of the parent 2,2'-bipyridin-3,3'-diamine (**3**, entry 1). A broad resonance, centered around 6.26 ppm and assigned to the NH_2 protons of diamine **3**, is observed in $CDCl_3$. The corresponding amide NH resonances of the diacetylated compounds are observed much more downfield, featuring sharp signals up to 14.97 ppm. The shift in NH is corroborated by a strong downfield shift of H-4 up to $\Delta\delta$ 2.4 ppm. Finally, the H-6 protons undergo the expected modest deshielding upon *N*-acylation, due to the more electron-withdrawing character of the the C-3 substituent. All these data are in good agreement with intramolecular hydrogen bonding between the amide function of one ring and the pyridine N-1 of the other (and *vice versa*). The hydrogen-donor ability (acidity and orientation) of the amide moiety apparently matches the hydrogen-acceptor behaviour of the pyridine N-1 perfectly, resulting in strong hydrogen bonding. The downfield shift of H-4 is explained by a coplanar orientation of the amide moiety with respect to the transoid bipyridine system, in which the carbonyl, pointing to H-4, exerts a downfield anisotropic effect.

In addition we compared acylated bipyridin-3-amines with acylated mono-pyridin-3-amines. Figure 3 compares the ^1H NMR spectrum of **1b** (Table I) with that of its "monomeric" counterpart **7a**, which lacks the possibility of intramolecular hydrogen bonding (Table II). The amide protons in **1b** feature a relative deshielding of 6.87 ppm while H-4 in **1b** shows only a deshielding of 1.1 ppm. Therefore the position of the NH signals is an important parameter in determining the strength of the hydrogen bonding; moreover the relative position of H-4 is indicative of the structures presented here.

In the case of the quinoline-8-carbonyl derivatives **1d** and **7c** (entries 5 and 13) the amide proton of the monomeric counterpart **7c** also features a low field resonance for the NH proton (13.89 ppm) indicating that intramolecular hydrogen bonding is present (Figure 4). More specific ^1H NMR data comparing **1d** and **7c**, are given in Table IV. It is clear from the low field absorption of H-4 (9.31 ppm) in compound **1d** that the amide group is positioned in the plane of the pyridine unit. In compound **7c**, however, the pyridine ring is free to rotate which results in the relatively low value for H-4 (8.52 ppm). Another remarkable effect is the relative shielding of H-2' in **1d** when compared with the corresponding proton in **7c**. We suppose that some repulsion between H-6 of the pyridine and H-2' of the quinoline ring forces the latter to some extent out of coplanarity, resulting in less deshielding of H-2' by the pyridine ring and explaining the upfield shift from 9.04 ppm in **7c** to 8.55 ppm in **1d**. In contrast to H-2', the chemical shifts of H-7' in **1d** (δ 8.75 ppm) and **7c** (δ 8.95 ppm) do not differ significantly, presumably due to the smaller effect of rotation about the C-8'–C=O bond on the distance between H-7' and the carbonyl moiety. The ^1H NMR data of **1d** are consistent with a structure incorporating two bifurcated hydrogen bonds.

From Table I and taking into account resonance structures, we can deduce that hydrogen bond strength and acidity of the NH are interrelated. This is demonstrated for the compounds **1a** and **1h**; the amide protons in **1a** [δ(NH) 13.12 ppm] are more acidic than the urea protons in **1h** [δ(NH) 12.57 ppm] due to cross-conjugation in the latter. As mentioned above, also the position of H-4 is an important probe to study the coplanarity. In the amide group, the C–N bond has more double bond character than in the urea group. Therefore, the carbonyl in the latter has a lower degree of coplanarity with the pyridine ring, as is expressed by the δ values assigned to H-4 in compounds **1a** (9.06 ppm) and **1h** (8.86 ppm), respectively. A similar deduction can be made for amide and acylurea compounds as is exemplified by the comparison of **1c** [δ(NH) 14.11 and δ(H-4) 9.35] with **1j** [δ(NH) 13.28 and δ(H-4) 8.79].

The discussion so far has been focussed on intramolecular hydrogen bonding, ignoring the possibilities of intermolecular interactions. Concentration dependent ^1H NMR

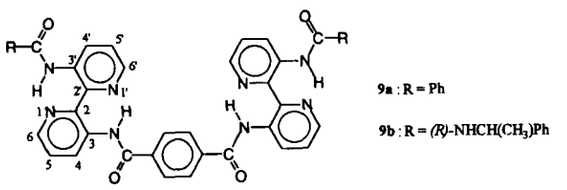


Figure 2. Dimeric oligomers.

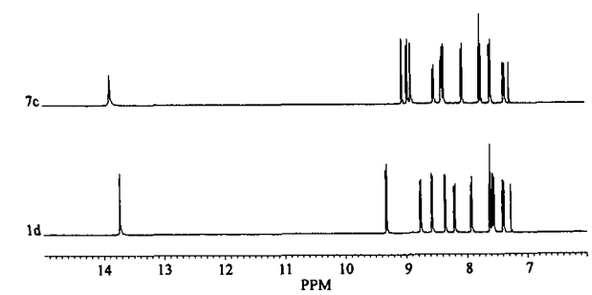
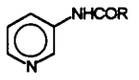
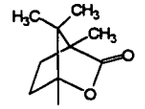
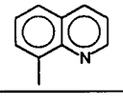


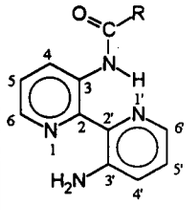
Figure 4. Comparison of 3,3'-bis(quinoline-8-carbonylamino)-2,2'-bipyridine (**1d**) *with its monomeric counterpart* **7c**.

Table II Acylated aminespyridines; relevant ^{1}H-NMR data [a]

Entry	Compound		Yield (%)	δ (N-H)	δ (H–4)	δ (H-6)
		R =				
12	**7a**		60	8.08	8.32	8.38
13	**7b**		60	8.24	8.14	8.42
14	**7c**		46	13.88	8.52	8.37

[a] All δ values are expressed in ppm and were measured in $CDCl_3$.

Table III Monoacylated 3,3'-diamines-2,2'-bipyridine and their ^{1}H-NMR characteristics [a]

Entry	Compound		Yield (%)	δ (N-H; NH2)	δ (H-4; H-4')	δ (H-6; H-6')
		R =				
15	**8a**	Ph	33	14.74; 6.62	9.30; 7.11	8.32; 8.00
16	**8b**	*(R)*-NHCH(CH$_3$)Ph	87	12.70; 6.45	8.84; 7.08	8.20; 7.86

[a] All δ values are expressed in ppm and were measured in $CDCl_3$

Table IV Comparison of the NMR data of **1d** *and* **7c**[a].

δ	**1d**	**7c**
δ(N-H)	**13.74**	**13.89**
δ(H-2)	/	8.89
δ(H-4)	**9.30**	**8.53**
δ(H-6)	8.35	8.39
δ(H-2')	**8.55**	**9.04**
δ(H-7')	8.75	8.95

[a] All values are given in ppm and were measured in $CDCl_3$.

Table V Influence of the medium on the hydrogen bonding in **1b**[a].

medium	δ(NH)	δ(H-4)	δ(H-6)
$CDCl_3$	14.60	9.42	8.40
toluene-d_8	14.70	9.70	8.00
DMSO-d_6	14.24	9.25	8.63
$CD_3COOD/CDCl_3$ 3/1	(14.60)	9.37	8.46
$CDCl_3$/TFA 3/1	9.90	8.95	8.80
$CDCl_3$/DMAP 3/1	14.60	9.42	8.40

[a] All values are given in ppm.

spectra of dihexanoyl derivative **1a** in $CDCl_3$ do not show significant chemical shift variations: the δ values for the NH and H-4() protons range from 13.197 (0.15 M) to 13.193 (0.015 M) ppm and 9.149 (0.15 M) to 9.150 (0.015 M) ppm, respectively. The urea and acylurea compounds **1g-j** do, in principle, have extra possibilities for intermolecular hydrogen bonding. However, in the ^{1}H NMR spectra, we do not observe any evidence for an association in solution. The insolubility of dibenzoylurea **1i** on the contrary indicates intermolecular hydrogen bonding in the crystalline state. X-ray studies are in progress to investigate this topic.

3. Strength of hydrogen bonding: medium and temperature effects

In order to investigate the strength of the hydrogen bonds in more detail, we have studied the ^{1}H NMR data as a function of medium and temperature. Table V gives relevant ^{1}H NMR data of compound **1b** in various solvents. The position of the amide proton in **1b** is unaffected by all the investigated solvents except TFA [a]. Apparently, even strong proton acceptors like DMSO do not break the hydrogen bonds, neither acetic acid nor DMAP [b] is capable of affecting the intramolecular hydrogen bonding.

These results allow us to conclude that, as long as the compounds are in a neutral state, the hydrogen bonds are retained. In contrast, the hydrogen bonds break as a result of salt formation in TFA. The addition of a base like triethylamine restores the hydrogen bonding. This protonation/deprotonation might be a useful principle to

[a] TFA = trifluoroacetic acid.
[b] DMAP = 4-(dimethylamino)pyridine.

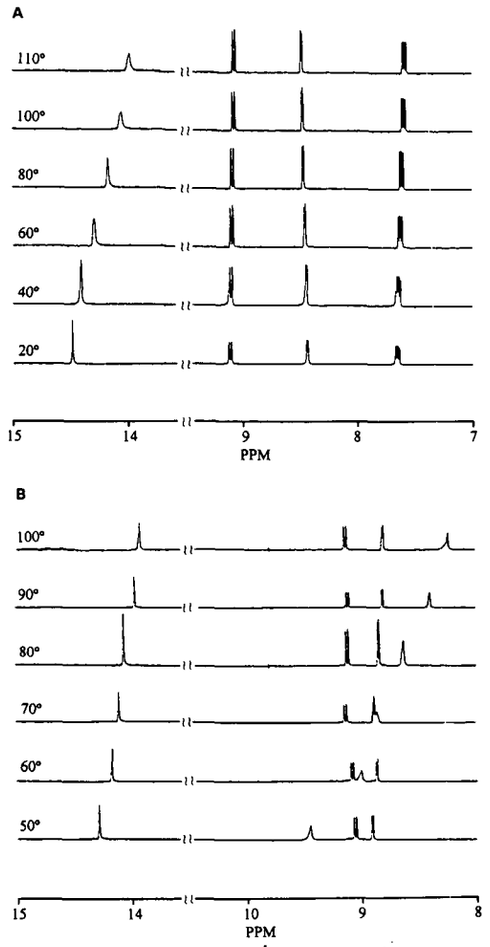


Figure 5a-b. Variable-temperature ^1H NMR of (a) compound **1e** *in DMSO-d_6 and (b) compound* **1j** *in toluene-d_8.*

induce reversibly the secondary structure in this bipyridine diamine unit.

Figure 5a shows variable temperature ^1H NMR measurements of compound **1e** in DMSO-d_6. There is some weakening of the hydrogen bonding as expressed by the upfield shift of the amide resonance on an increase of temperature ($\Delta\delta/\Delta T = 5.8 \cdot 10^{-3}$ ppm/K). But even at higher temperatures (110°C) the secondary hydrogen bonds do not collapse. Other compounds (entries 4–6) have also been measured and show similar behaviour. The strength of intramolecular hydrogen bonding is also illustrated in acylurea **1j** (Figure 5b); the amide NH is hardly

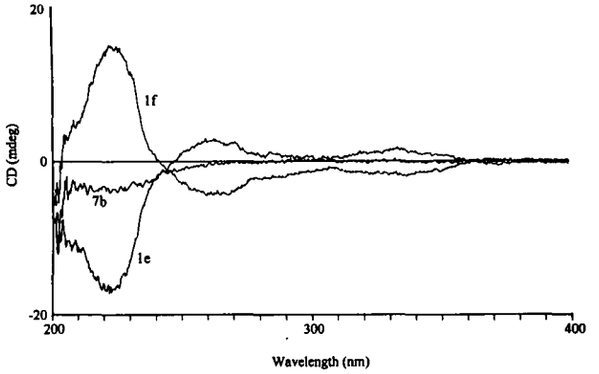


Figure 6. CD spectra of (+) and (−)-3,3'-bis(camphanoylamino)-2,2'-bipyridine (**1e-f**) *and (−)-3-(camphanoylamino)pyridine* (**7b**) *recorded in MeOH.*

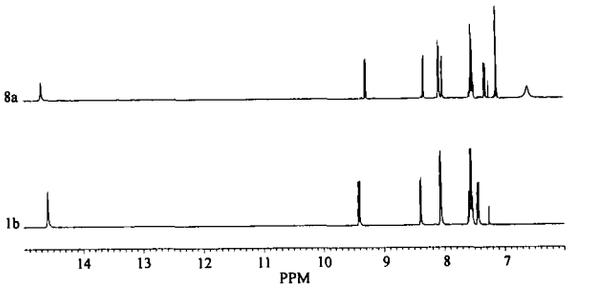


Figure 7. Comparison of compounds **1b** *and* **8a**: *influence of single and double H-bonding in 2,2'-bipyridine-3,3'-diamines.*

affected by raising the temperature ($\Delta\delta/\Delta T = 7 \cdot 10^{-3}$ ppm/K) while the imide NH shifts from 9.5 ppm (50°C) to 8.3 ppm (100°C) ($\Delta\delta/\Delta T = 24 \cdot 10^{-3}$ ppm/K). Comparison of our data with some temperature-dependent measurements, reported by *Hamilton* et al.[5] in an unspecified temperature range ($\Delta\delta/\Delta T = 3.0 \cdot 10^{-3}$ and $1.5 \cdot 10^{-3}$ ppm/K), illustrate the strength of the intramolecular hydrogen bonding in the compounds presented in this paper. Finally, it is worth noting that the resonance of H-4 is independent of the temperature which again indicates the retention of coplanarity of most parts of the molecule.

4. Optical activity of 2,2'-bipyridines

In order to investigate the coplanarity of the bipyridines, we recorded UV and CD [c] spectra of the optically active bipyridine derivatives **1e** and **1f**, while pyridine derivative **7b** was used as a monomeric reference compound. The UV spectra of the bipyridines show λ_{max} at 226, 267 and 336 nm in MeOH. The CD spectra of the three optically active products are recorded in MeOH and are represented in Figure 6. The expected mirror image relationship between **1e** and **1f** is observed and all three absorption bands exhibit a Cotton effect. No evidence for exciton coupling can be found in the spectra. The λ_{max} 336 nm transition is attributed to the bipyridine unit. The presence of a small Cotton effect in this band can be indicative for a minor deviation from coplanarity of the two pyridine rings in solution. The behaviour in the solid phase is under investigation and will be derived from X-ray measurements in appropriate crystals.

5. Cooperativity

Figure 7 gives the ^1H NMR spectra of diacylated compound **1b** and monoacylated compound **8a** recorded in $CDCl_3$. The NH signal in **8a** appears at the same chemical shift as that of the NH for the corresponding diacylated compound **1b**. Variable-temperature (20–100°C) ^1H NMR experiments of compound **8a** in DMSO show a temperature-independent behaviour similar to that observed for compound **1b** ($\Delta\delta/\Delta T = 5.125 \cdot 10^{-3}$ ppm/K). These phenomena imply that cooperativity is not needed to induce coplanarity in the bipyridine structure. Moreover, the NH resonance of **8a** (14.74 ppm) is even more downshifted than the NH resonance of **1b** (14.59). An explanation can be offered by considering the hydrogen-donor and hydrogen-acceptor abilities of NHCO and pyridine N-1, respectively. Indeed, acylation of a pyridinamine ring enhances the hydrogen-donor but diminishes the hydrogen-acceptor ability of that ring.

[c] CD = circular dichroism.

Conclusions

The ^{1}H NMR results of a series of mono- and diacylated 2,2'-bipyridine-3,3'-diamines show the presence of strong intramolecular hydrogen bonds, leading to coplanar structures. Evidence is presented that the NHCO group is always coplanar with the bipyridine unit. Upon incorporation of the quinoline-8-carbonyl group in the structure the CONH group shares, as hydrogen bond donor, its hydrogen with both the pyridine and the quinoline hydrogen-bond acceptors, leading to bifurcated secondary structures. The intrinsic strength of the intramolecular hydrogen bonding is demonstrated under various conditions, such as high temperature and polar protic solvents. Only the addition of TFA leads to hydrogen bond collapse due to protonation, but the addition of a strong base restores the hydrogen bonds. The cooperativity in hydrogen bonding predicted for the diacylated 2,2'-bipyridine-3,3'-diamines has not been observed under the conditions studied so far. One intramolecular hydrogen bond is sufficient to force the bipyridine to coplanarity, as has been demonstrated with monoacylated bipyridines. The strong intramolecular hydrogen bonds present in acylated 2,2'-bipyridine-3,3'-diamines are expected to make them promising building blocks for the construction of two-dimensional supramolecular architectures.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 (400.13 MHz for ^{1}H NMR and 100.62 for ^{13}C NMR). Infrared spectra were recorded on a Perkin Elmer 1605 FT-IR and UV spectra measured on a Perkin-Elmer Lambda 3B UV-VIS spectrometer. CD measurements were effected on a Jasco J-600 spectropolarimeter. Melting points were recorded with an Unkam THMS 600 heating device. Elemental analyses were carried out using a Perkin Elmer 240. Diethyl ether was dried on $CaCl_2$ and stored on sodium wire, THF was distilled from Na/benzophenone and CH_2Cl_2 was dried on $CaCl_2$ and distilled from P_2O_5. Benzoyl isocyanate[8] and quinoline-8-carbonyl chloride[9] were prepared according to standard procedures.

3,3'-Dinitro-2,2'-bipyridine (**2**)[7]

Copper bronze (40 g, 0.63 mol) and 2-chloro-3-nitropyridine (40 g, 0.25 mol) in DMF (200 ml) were heated at 100°C. The reaction was monitored by TLC (eluent: toluene/EtOAc 1/1) and took between one and several hours due to the induction period. When all starting material had disappeared, the reaction mixture was poured into water (300 ml), the remaining precipitates filtered off and washed with water (3×50 ml). Soxhlet extraction for 4 days with CH_3CN (500 ml) of the solid residue, evaporation of the solvent *in vacuo* and treatment of the resulting solids with 10% ammonia solution to remove Cu salts yielded after filtration **2** as a yellow powder (24 g, 78%, lit.[7] 51%). Recrystallization from CH_3CN gave an analytically pure sample; m.p. 210–211°C (lit.[7] 206°C). ^{1}H NMR (DMSO): 8.94 (dd, 2H, *J* 1.4 and 4.8 Hz, H-6); 8.72 (dd, 2H, *J* 1.4 and 8.4 Hz, H-4); 7.89 (dd, 2H, *J* 4.8 and 8.3 Hz, H-5). ^{13}C NMR: 153.0 (C-6); 149.2 (C-3); 144.6 (C-2); 133.8 (C-4); 125.4 (C-5). Anal. calcd. for $C_{10}H_6N_4O_4$ (246.18): C 48.79, H 2.45, N 22.76; found: C 48.9, H 2.7, N 22.9%.

2,2'-Bipyridine-3,3'-diamine (**3**)[6a]

The synthesis was accomplished according to the previously described procedure. After recrystallization from water pure **3** was obtained as yellow needles (3.17 g, 70%, lit.[6a] 70.6%); m.p. 136.5–137.5°C, lit.[6a] 133–135°C. ^{1}H NMR ($CDCl_3$): 7.96 (dd, 2H, *J* 2.2 and 3.7 Hz, H-6); 7.02 (m, 4H, H-4 and H-5); 6.26 (bs, 4H, NH). ^{13}C NMR: 143.7 (C-3); 140.5 (C-2); 135.7 (C-6); 123.9 (C-4); 122.9 (C-5). Anal. calcd. for $C_{10}H_{10}N_4$ (186.22): C 64.50, H 5.41, N 30.09; found: C 65.6, H 5.4, N 30.3%.

General procedure for the acylation of **3** *with acid chlorides*

To an ice-cooled and stirred solution of **3** and TEA[d] (2 eq.) in dry diethyl ether (0.1 M) under argon atmosphere, a solution of the acid chloride (2 eq.) in dry diethyl ether (0.2 M) was added dropwise. After 1 h the ice bath was removed and stirring was continued until TLC showed the absence of the starting materials.

3,3'-Bis(hexanoylamino)-2,2'-bipyridine (**1a**)
After stirring at room temperature for 2 h the precipitates were filtered, washed with water to remove the TEA salt, dried and recrystallized from MeOH to yield pure **1a** as cream-coloured plates (0.30 g, 73%); m.p. 107–108°C. ^{1}H- NMR ($CDCl_3$): 13.12 (s, 2H, NH); 9.06 (dd, 2H, *J* 1.7 and 8.5 Hz, H-4); 8.25 (dd, 2H, *J* 1.7 and 4.3 Hz, H-6); 7.30 (dd, 2H, *J* 4.6 and 8.5 Hz, H-5); 2.37 (t, 4H, $COCH_2$); 1.70 (qui, 4H, $COCH_2CH_2$); 1.31 (m, 8H, $CH_2CH_2CH_3$); 0.82 (t, 6H, CH_3). ^{13}C NMR: 172.6 (CO); 141.9 (C-2); 140.2 (C-6); 136.7 (C-3); 129.9 (C-4); 123.9 (C-5); 38.7 ($COCH_2$); 31.3 ($COCH_2CH_2$); 25.2 ($CH_2CH_2CH_3$); 22.4 (CH_2CH_3); 13.9 (CH_3). Anal. calcd. for $C_{22}H_{30}N_4O_2$ (382.52): C 69.08, H 7.90, N 14.65; found: C 68.6, H 7.5, N 14.8%.

3,3'-Bis(benzoylamino)-2,2'-bipyridine (**1b**)
After stirring at room temperature for 2 h the precipitates were filtered, washed with water to remove the TEA salt, dried and recrystallized from CH_3CN to yield pure **1b** as light-yellow needles (0.26 g, 62%); m.p. 236.8–238.3°C. ^{1}H NMR ($CDCl_3$): 14.59 (s, 2H, NH); 9.42 (dd, 2H, *J* 1.7 and 8.5 Hz, H-4); 8.41 (dd, 2H, *J* 1.3 and 4.4 Hz, H-6); 8.07 (d, 4H, H-*ortho*); 7.58 (m, 6H, H-*meta* and *para*); 7.46 (dd, 2H, *J* 4.4 and 8.5 Hz, H-5). ^{13}C NMR ($CDCl_3$): 166.4 (CO); 142.0 (C-2); 140.2 (C-6); 137.6 (C-2); 135.3 (C-*ipso*); 132.0 (C-*para*); 129.9 (C-4); 128.8 (C-*ortho*); 127.4 (C-*meta*); 124.2 (C-5). Anal. calcd. for $C_{24}H_{18}N_4O_2$ (394.72): C 73.08, H 4.60, N 14.20; found: C 73.3, H 5.0, N 14.0%.

3,3'-Bis[3,4,5-tris(dodecyloxy)benzoylamino]-2,2'-bipyridine (**1c**)[10]
The mixture was stirred at room temperature for 3 h and then filtered. The filtrate was evaporated *in vacuo* to give crude **1c**. The resulting solids were dissolved in $CHCl_3$ (15 ml). Extraction with water (3×10 ml) and brine (10 ml) and evaporation of the organic phase *in vacuo* also gave **1c**. The combined crops of **1c** were recrystallized from EtOAc to yield pure **1c** as a light yellow powder (0.52 g, 72%); m.p. 124.3–124.8°C. ^{1}H NMR ($CDCl_3$): 14.11 (s, 2H, NH); 9.35 (dd, 2H, *J* 1.6 and 8.5 Hz, H-4); 8.38 (dd, 2H, *J* 1.4 and 4.6 Hz, H-6); 7.44 (dd, 2H, *J* 4.6 and 8.5 Hz, H-5); 7.25 (s, 4H, H-*ortho*); 4.05 (m, 12H, OCH_2); 1.85 (qui, 8H, OCH_2CH_2-*meta*); 1.77 (qui, 4H, OCH_2CH_2-*para*); 1.50 (qui, 12H, $OCH_2CH_2CH_2$); 1.31 (bs, 96H, $(CH_2)_8$); 0.88 (t, 18H, CH_3). Anal. calcd. for $C_{96}H_{162}N_4O_8$ (1500.36): C 76.85, H 10.88, N 3.73;. found: C 76.4, H 11.1, N 3.4%.

3,3'-Bis(quinoline-8-carbonylamino)-2,2'-bipyridine (**1d**)
Due to the poor solubility of quinoline-8-carbonyl chloride·hydrochloride in diethyl ether, CH_2Cl_2 was used as solvent. Four equivalents of TEA were used. After stirring for 4 h at room temperature the suspension was extracted with water (3×35 ml) and brine (35 ml) and the organic phase was dried with $MgSO_4$ and evaporated *in vacuo*. The resulting oil was purified by column chromatography (SiO_2; first CH_3CN/CH_2Cl_2 1/1 to remove impurities, then CH_2Cl_2/MeOH 95/5 to elute the amide **1d**) and triturated with MeOH to yield **1d** as a beige powder (0.25 g, 38%); m.p. 225–227°C. ^{1}H NMR ($CDCl_3$): 13.74 (s, 2H, NH); 9.31 (dd, 2H, *J* 1.5 and 8.5 Hz, H-4); 8.76 (dd, 2H, *J* 1.4 and 7.4 Hz, H-7'); 8.57 (dd, 2H, *J* 1.4 and 4.6 Hz, H-2'); 8.35 (dd, 2H, *J* 1.7 and 4.3 Hz, H-6); 8.20 (dd, 2H, *J* 1.5 and 8.4 Hz, H-4'); 7.92 (d, 2H, *J* 8.1 Hz, H-5'); 7.61 (t, 2H, *J* 7.7 Hz, H-6'); 7.55 (dd, 2H, *J* 4.6 and 8.4 Hz, H-3'); 7.40 (dd, 2H, *J* 4.3 and 8.2 Hz, H-5). ^{13}C NMR: 164.59 (CO); aromatic carbons: 153.0; 149.0; 147.4; 145.0; 144.2; 137.6; 135.3; 134.0; 132.5; 130.3; 128.3; 126.4; 123.9; 120.9. Anal. calcd. for $C_{30}H_{20}N_6O_2$ (496.53): C 72.57, H 4.06, N 16.92%; found: C 72.0, H 4.2, N 17.0%.

(+)-3,3'-Bis(camphanoylamino)-2,2'-bipyridine (**1e**)
(−)-Camphanoyl chloride was used. After stirring at room temperature for 2 h, the solids were filtered and washed with hot diethyl ether. The filtrate was evaporated *in vacuo* and the resulting solid was recrystallized from MeOH to yield pure **1e** as light yellow

[d] TEA = triethylamine.

needles (0.60 g, 68%); m.p. 281–282.5°C; $[\alpha]_D^{24}$ 84.4° ($CHCl_3$, *c* 0.64). ^1H NMR ($CDCl_3$): 14.97 (s, 2H, NH); 9.22 (dd, 2H, *J* 1.4 and 8.5 Hz, H-4); 8.58 (dd, 2H, *J* 1.5 and 4.5 Hz, H-6); 7.40 (dd, 2H, *J* 4.5 and 8.5 Hz, H-5); 2.64 (m, 2H); 2.02 (m, 4H); 1.77(m, 2H); 1.16 (s, CH_3-*syn*); 1.14 (s, CH_3-*anti*); 0.93 (s, CH_3-C-3). ^{13}C NMR ($CDCl_3$); 178.23 (CO, lactone); 166.73 (CO, amide); 141.61 (C-2); 141.32 (C-6); 135.98 (C-3); 129.18 (C-4); 124.21 (C-5); sp^3 carbons: 92.8; 55.4; 54.4; 30.1; 29.1; 16.7; 16.6; 9.8. Anal. calcd. for $C_{30}H_{34}N_4O_6$ (546.65): C 65.91, H 6.27, N 10.24; found: C 66.3, H 6.5, N 10.3%.

(−)-3,3'-Bis(camphanoylamino)-2,2'-bipyridine (**1f**)
(+)-Camphanoyl chloride was used. Compound **1f** was obtained according to the procedure applied for **1e**; yield 0.17 g (70%); m.p. 281–283°C; $[\alpha]_D^{24}$ −83.7° ($CHCl_3$, *c* 0.54). Anal. calcd. for $C_{30}H_{34}N_4O_6$ (546.65): C 65.91, H 6.27, N 10.24; found: C 65.6, H 6.5, N 10.1%.

Procedures for the acylation of **3** *with isocyanates*

3,3'-Bis(3-phenylureido)-2,2'-bipyridine (**1g**)[6a]
Phenyl isocyanate (0.4 g, 3.35 mmol) and **3** (0.2 g, 1.08 mmol) were dissolved in toluene (8 ml) and stirred for 30 min at 80°C. After cooling, the resulting precipitate was filtered and the solids were suspended in hot MeOH (50 ml), filtered and dried to give a white powder (0.48 g, 80%, lit.[6a] 94.3%); m.p. 221–224°C, lit.[6a] 207–209°C. ^1H NMR (DMSO-d_6): 11.30 (s, 2H, NHCO); 9.65 (s, 2H, NHPh); 8.72 (dd, 2H, *J* 1.6 and 8.5 Hz, H-4); 8.39 (dd, 2H, *J* 1.4 and 4.6 Hz, H-6); 7.50 (m, 6H, H-5 and H-*ortho*); 7.31 (t, 4H, H-*meta*); 7.01 (t, 2H, H-*para*). ^{13}C NMR: 152.5 (CO); 142.3 (C-2); 140.7 (C-*ipso*); 139.5 (C-6); 136.0 (C-3); 129.8 (C-4); 128.7 (C-*meta*); 123.5 (C-5); 122.3 (C-*para*); 119.1 (C-*ortho*). Anal. calcd for $C_{24}H_{20}N_6O_2$ (424.46): C 67.91, H 4.75, N 19.80; found: C 67.8, H 4.7, N 19.8%.

3,3'-Bis(3-butylureido)-2,2'-bipyridine (**1h**)
Butyl isocyanate (0.26 ml, 2.3 mmol) and **3** (0.2 g, 1.08 mmol) were dissolved in toluene and stirred for 3 h at 80°C. After cooling, pentane (5 ml) was added to the solution, the solids were filtered and recrystallized from toluene to give pure **1h** as yellow plates (0.13 g, 34%); m.p. 201.5–204°C. ^1H NMR ($CDCl_3$): 12.57 (bs, 2H, NHCO); 8.86 (dd, 2H, *J* 1.3 and 7.8 Hz, H-4); 8.10 (dd, 2H, *J* 1.4 and 4.5 Hz, H-6); 7.20 (dd, 2H, *J* 4.5 and 8.5 Hz, H-5); 4.63 (bs, 2H, N*H*CH_2); 3.25 (qua, 4H, NHCH_2); 1.53 (qui, 4H, NHCH$_2$CH_2); 1.37 (se, 4H, CH_2CH$_3$); 0.90 (t, 6H, CH_3). ^{13}C NMR: 155.58 (CO); 141.4 (C-2); 138.4 (C-6); 137.7 (C-3); 128.9 (C-4); 123.6 C-5); 40.6 (NH*C*H$_2$); 32.1 (NHCH$_2$*C*H$_2$); 20.1 (*C*H$_2$CH$_3$); 13.8 (*C*H$_3$). Anal.calcd. for $C_{20}H_{28}N_6O_2$ (384.48): C 62.48, H 7.34, N 21.86; found: C 62.9, H 7.3, N 21.9%.

3'-[3-(α-Methylbenzyl)ureido]-2,2'-bipyridin-3-amine (**8b**)
R-(+)-α-Methylbenzyl isocyanate (0.3 ml) was added to a solution of **3** (0.32 g, 1.72 mmol) in toluene (7 ml) at 80°C. The solution was stirred for 2 h. After cooling, the resulting solids were filtered, washed with cold toluene and recrystallized from CH_3CN to give orange crystals (0.49 g, 87%); m.p. 208–210°C. ^1H NMR ($CDCl_3$): 12.70 (bs, 1H, NHCO); 8.84 (dd, 1H, *J* 1.7 and 8.5 Hz, H-4); 8.20 (dd, 1H, *J* 1.4 and 4.5 Hz, H-6); 7.86 (s, 1H, H-6'); 7.40 (m, 4H, H-*ortho* and -*meta*); 7.27 (t, 1H, H-*para*); 7.22 (dd, 1H, *J* 4.8 and 8.5 Hz, H-5); 7.08 (m, 2H, H-4' and H-5'); 6.45 (bs, 2H, NH_2); 5.04 (qui, 1H, CH); 4.80 (d, 1H, N*H*CH); 1.55 (d, 3H, CH_3). Anal. calcd for $C_{19}H_{19}N_5O$ (333.39): C 68.45, H 5.74, N 21.01; found: C 68.3, H 5.2, N 21.1%.

3'-(Benzoylamino)-2,2'-bipyridin-3-amine (**8a**)[6c]
The synthesis was accomplished according to previously described procedures[6c]. Recrystallization from CH_3CN yielded an analytically pure sample (0.99 g, 33%); m.p. 167.5–168.5°C, lit.[6c] 163–164°C. ^1H NMR ($CDCl_3$): 14.74 (s, 1H, NHCO); 9.30 (dd, 1H, *J* 1.5 and 8.3 Hz, H-4); 8.32 (dd, 1H, *J* 1.7 and 4.8 Hz, H-6); 8.08 (dt, 1H, H-*ortho*); 8.00 (dd, 1H, *J* 2.4 and 3.6 Hz, H-6'); 7.55 (m, 3H, H-*meta* and H-*para*); 7.30 (dd, 1H, *J* 4.6 and 8.4 Hz, H-5); 7.11 (m, 2H, H-4' and H-5'); 6.62 (bs, 2H, NH_2). ^{13}C NMR ($CDCl_3$): 166.2 (CO); aromatic carbons: 145.1; 143.5; 140.7; 138.4; 136.2; 135.6; 134.7; 131.6; 128.6; 128.4; 127.4; 125.2; 124.1; 122.6. Anal. calcd. for $C_{17}H_{11}N_4O$ (290.32): C 70.33, H 4.86, N 19.29; found: C 70.2, H 4.6, N 19.8%.

3,3'-[1,4-Phenylenebis(carbonylamino)]-bis(3'-benzoylamino-2,2'-bipyridine) (**9a**)
To a solution of **8a** (0.26 g, 1.0 mmol) and TEA (0.15 ml, 2 mmol) in dry THF (10 ml), a solution of benzene-1,4-dicarbonyl dichloride (85 mg, 0.41 mmol) in dry THF was added dropwise under argon atmosphere. After stirring at room temperature for 2 h, the solution was heated (60°C) for 15 min. After cooling, the resulting precipitates were filtered, washed with THF (3×5 ml) and water (3×15 ml) and dried *in vacuo*. Pure **9a** was obtained as a light yellow powder (0.20 g, 73%); m.p. > 300°C. ^1H NMR ($CDCl_3$/TFA 3/1): 10.72–9.83 (bs, 4H, NHCO); 8.97 (d, 2H, *J* 8.4 Hz, H-4); 8.85 (m, 4H, H-4' and H-6'); 8.79 (d, 2H, *J* 4.5 Hz, H-6); 8.15 (m, 4H, H-5 and H-5'); 7.89 (s, 4H, H-*ortho*); 7.70 (m, 6H, H'-*ortho* and H'-*para*); 7.50 (t, 4H, H'-*meta*). Anal. calcd. for $C_{42}H_{30}N_8O_4$ (710.75): C 70.90, H 4.25, N 15.76; found: C 70.3, H 4.2, N 15.9%.

3,3'-[1,4-Phenylenebis(carbonylamino)]-bis[3'-(R-α-methylbenzyl)-ureido-2,2'-bipyridine] (**9b**)
To a solution of **8b** (0.2 g, 0.6 mmol) and TEA (0.1 ml, 1.2 mmol) in dry CH_2Cl_2/THF (1/1, 20 ml), a solution of benzene-1,4-dicarbonyl dichloride (55 mg, 0.27 mmol) in dry THF (3 ml) was added dropwise under argon atmosphere. After stirring at room temperature for 16 h, the solvent was evaporated *in vacuo*. The resulting solids were suspended in a saturated $NaHCO_3$ solution, stirred for 30 min, filtered, washed thoroughly with water and dried. Recrystallization from THF yielded pure **9b** as a white powder (100 mg, 48%); m.p. > 300°C. ^1H NMR (DMF-d_7): 14.49 (s, 2H, amide-NH); 12.28 (s, 2H, urea-NH); 9.29 (d, 2H, *J* 8.5 Hz, H-4); 9.03 (d, 2H, *J* 8.5 Hz, H-4'); 8.57 (dd, 2H, *J* 3.8 and 1.4 Hz, H-6'); 8.53 (dd, 2H, *J* 3.5 and 1.2 Hz, H-6); 8.33 (s, 4H, H-*ortho*); 8.02 (bs, 2H, *H*NCH(CH$_3$)Ph); 7.60 (dd, 2H, *J* 4.5 and 8.5 Hz, H-5); 7.53 (dd, 2H, *J* 4.5 and 8.5 Hz, H-5'); 7.44 (d, 4H, H'-*ortho*); 7.34 (t, 4H, H'-*meta*); 7.25 (t, 2H, H'-*para*); 5.01 (q, 2H, *H*C(CH$_3$)Ph); 1.47 (d, 6H, CH_3). Anal calcd. for $C_{46}H_{40}N_{10}O_4$ (796.88): C 69.33, H 5.06, N 17.56; found: C 69.6, H 5.0, N 17.3%.

3,3'-Bis(3-benzoylureido)-2,2'-bipyridine (**1i**)
To benzoyl isocyanate (0.3 g, 2 mmol) in dry CH_2Cl_2 (6 ml), a solution of **3** (0.18 g, 1 mmol) in dry CH_2Cl_2 (6 ml) was added dropwise under argon. After stirring for 4 h at 30–40°C the solvent was evaporated *in vacuo* and the solids were triturated with hot CH_3CN (2×30 ml) to yield **1i** as a cream coloured powder (0.34 g, 70%); m.p. 279–282°C (dec.). ^1H NMR ($CDCl_3$/TFA 3/1): 10.18 (bs, 4H, NH); 9.23 (d, 2H, *J* 8.6 Hz, H-4); 8.96 (d, 2H, *J* 5.2 Hz, H-6); 8.28 (dd, 2H, *J* 5.4 and 8.5 Hz, H-5); 7.88 (d, 4H, H-*ortho*); 7.72 (t, 2H, H-*para*); 7.56 (t, 4H, H-*meta*). ^{13}C NMR: 171.0 (CO); 154.3 (CO); 142.4; 141.3; 137.3; 135.7; 135.1; 130.2; 129.7; 129.6; 128.3.

3,4,5-Tris(dodecyloxy)benzamide (**5**)
In a separating funnel 3,4,5-tris(dodecyloxy)benzoyl chloride[10] (2 g, 2.9 mmol) was dissolved in dry diethyl ether (15 ml). A 25% solution of NH_3 in water (20 ml) and ice (20 g) was added and the mixture was shaken vigorously. The resulting white precipitate was filtered, washed with water and dried to yield pure **5** (1.84 g, 95%). An analytical pure sample was obtained by recrystallization from hexane; m.p. 81–82.5°C. ^1H NMR ($CDCl_3$): 7.08 (s, 2H, H-*ortho*); 4.07 (t, 6H, OCH_2); 1.85 (m, 6H, OCH$_2$CH_2); 1.53 (qui, 6H, OCH$_2$CH$_2$CH_2); 1.34 (bs, 48H, (CH_2)$_8$); 0.95 (t, 9H, CH_3). Anal. calcd. for $C_{43}H_{79}NO_4$ (674.1): C 76.62%, H 11.81%, N 2.08%; found: C 76.5, H 11.8, N 2.0%.

3,4,5-Tris(dodecyloxy)benzoyl isocyanate (**6**)
To a suspension of **5** (1 g, 1.48 mmol) in 1,2-dichloroethane (20 ml) oxalyl chloride (0.45 g, 5 mmol) was added dropwise under argon. The suspension was stirred at 40–45°C for 48 h. The solvent and excess of oxalyl chloride were evaporated *in vacuo* and the resulting oil was used without further purification. ^1H NMR ($CDCl_3$): 7.17 (s, 2H, H-*ortho*); 4.05 (m, 6H, OCH_2); 1.78 (m, 6H, OCH$_2$CH_2); 1.49 (bs, 6H, OCH$_2$CH$_2$CH_2); 1.30 (bs, 48H, (CH_2)$_8$); 0.89 (t, 9H, CH_3).

3,3'-Bis[3[3,4,5-tris(dodecyloxy)benzoyl]ureido]-2,2'-bipyridine (**1j**)
To the solution of **6** in dry CH_2Cl_2 (6 ml), a solution of **3** (79 mg, 0.42 mmol) in dry CH_2Cl_2 (3 ml) was added dropwise. After stirring for 1 h at room temperature the solvent was evaporated *in vacuo* and the remaining brown solid was purified by column chromatography (SiO_2; eluent: CH_2Cl_2/MeOH 97.5/2.5) to yield pure **1j** as a white powder (0.38 g, 57%). An analytically pure sample was obtained by recrystallization from EtOAc/$CHCl_3$ (1/1). M.p. 126–127.5°C. ^1H NMR ($CDCl_3$): 13.28 (s, 2H, NHCO); 8.79 (dd, 2H, *J* 1.2 and 8.4 Hz, H-4); 8.69 (dd, 2H, *J* 1.4 and 4.7 Hz, H-6); 8.29 (bs, 2H, CONHCO); 7.42 (dd, 2H, *J* 4.5 and 8.4 Hz, H-5); 7.05 (s, 4H, H-*ortho*); 4.03 (t, 12H, OCH_2); 1.78 (m, 12H, OCH$_2$CH_2); 1.47 (qui, 12H, OCH$_2$CH$_2$CH_2); 1.27 (bs, 96H, (CH_2)$_8$); 0.88 (t, 18H, CH_3). Anal. calcd. for $C_{98}H_{164}N_6O_{10}$ (1586.40): C 74.20, H 10.42, N 5.30; found: C 73.9, H 10.6, N 5.2%.

General procedure for the acylation of pyridin-3-amine with acid chlorides

To an ice-cooled and stirred solution of pyridin-3-amine and TEA (1 eq.) under argon atmosphere in dry diethyl ether (0.2 M), a solution of the acid chloride (1 eq.) in dry diethyl ether (0.2 M) was added dropwise. After 1 h the ice bath was removed and stirring was continued until TLC confirmed the disappearance of the starting materials.

3-(Benzoylamino)pyridine (**7a**)
After stirring for 3 h the diethyl ether was evaporated *in vacuo*, CH_2Cl_2 (40 ml) was added and the solution was extracted with water (3×30 ml) and brine (20 ml). The solvent was evaporated *in vacuo* and the resulting solid was triturated with hot diethyl ether (2×10 ml) to remove impurities. Recrystallization of the residue from water yielded pure **7a** as white needles (1.34 g, 60%); m.p. 118.3–119°C. ^{1}H NMR ($CDCl_3$): 8.68 (d, 1H, *J* 2.4 Hz, H-2); 8.43 (s, 1H, NH); 8.35 (dd, 2H, *J* 1.3 and 4.7 Hz, H-6); 8.30 (ddd, 1H, *J* 1.5, 2.5, and 8.5 Hz, H-4); 7.90 (d, 2H, H-*ortho*); 7.58 (t, 1H, H-*para*); 7.49 (t, 2H, H-*meta*); 7.33 (dd, 1H, *J* 4.7 and 8.5 Hz, H-5). ^{13}C NMR: 166.6 (CO); 145.4 (C-6); 141.5 (C-2); 134.9 (C-*ipso*); 134.2 (C-3); 132.2 (C-*para*); 128.6 (C-*ortho*); 127.7 (C-4); 127.2 (C-*meta*); 123.7 (C-5). Anal. calcd. for $C_{12}H_{10}N_2O$ (198.22): C 72.71, H 5.08, N 14.13; found: C 73.0, H 5.3, N 14.1%.

(−)-3-(Camphanoylamino)pyridine (**7b**)
(−)-Camphanoyl chloride was used. After stirring for 2 h at room temperature, the reaction mixture was filtered. The filtrate was evaporated *in vacuo* and purified using column chromatography (SiO_2; eluent: CH_3CN/CH_2Cl_2 1/1) to give crude **7b**. The residue was washed with water to remove the TEA salt and gave a second crop of **7b**. The combined solids were recrystallized from water to give pure **7b** as white needles (0.70 g, 60%); m.p. 141.5–143°C. $[\alpha]_D^{25}$ −25.6° ($CHCl_3$, *c* 1.69). ^{1}H NMR ($CDCl_3$): 8.72 (d, 1H, *J* 2.5 Hz, H-2); 8.42 (dd, 1H, *J* 1.4 and 4.7 Hz, H-6); 8.24 (s, 1H, NH); 8.14 (ddd, 1H, *J* 1.5 and 2.6 and 8.4 Hz, H-4); 7.30 (dd, 1H, *J* 4.7 and 8.4 Hz, H-5); 2.60 (m, 1H); 2.04 (m, 2H); 1.76 (m, 1H); 1.17 (s, CH_3); 1.16 (s, CH_3); 1.00 (s, CH_3). ^{13}C NMR: 177.7 (CO, lactone); 165.8 (CO, amide); 146.1 (C-6); 141.5 (C-2); 133.6 (C-3); 127.1 (C-4); 123.62 (C-5); sp^3 carbons: 92.2; 55.4; 54.5; 30.5; 29.0; 16.7; 16.5; 9.7. Anal. calcd. for $C_{15}H_{18}N_2O_3$ (274.32): C 65.67, H 6.61, N 10.21; found: C 65.2, H 7.0, N 10.1%.

3-(Quinoline-8-carbonylamino)pyridine (**7c**)
THF was used instead of diethyl ether for reasons of low solubility and the acid chloride.hydrochloride was used: hence 2 eq. of TEA were needed. After stirring at 50–60°C for 5 h, the precipitates were filtered and washed with THF. The combined filtrates were evaporated *in vacuo* and the remaining solid was purified using column chromatography (SiO_2; eluent: CH_2Cl_2/CH_3CN 1/1). Recrystallization from water/MeOH 90/10 yielded **7c** as a white powder (0.15 g, 46%); m.p. 116.5–118.5°C. ^{1}H NMR ($CDCl_3$): 13.88 (s, 1H, NH); 9.04 (dd, 1H, *J* 1.8 and 4.2 Hz, H-2'); 8.95 (dd, 1H, *J* 1.3 and 7.4 Hz, H-7'); 8.88 (d, 1H, *J* 2.2 Hz, H-2); 8.52 (m, 1H, H-4); 8.37 (m, 2H, H-4' and H-6), 8.05 (dd, 1H, *J* 1.5 and 8.1 Hz, H-5'); 7.75 (t, 1H, *J* 7.7 Hz, H-6'); 7.59 (dd, 1H, *J* 4.3 and 8.4 Hz, H-3'); 7.35 (dd, 1H, *J* 4.7 and 8.3 Hz, H-5). ^{13}C NMR: 164.2 (CO); aromatic carbons: 149.2; 145.3; 144.9; 142.0; 138.2; 135.8; 134.4; 132.7; 128.6; 128.1; 127.5; 126.8; 123.7; 121.2. Anal. calcd. for $C_{15}H_{11}N_3O$ (249.27): C 72.28, H 4.45, N 16.68; found: C 71.9%, H 4.7, N 16.6%.

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