Helicity-Encoded Molecular Strands: Efficient Access by the Hydrazone Route and Structural Features

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Dedicated to Professor *Jack D. Dunitz* on the occasion of his 80th birthday

Control over the folding of molecular strands may be achieved by appropriate choice of the constituting subunits, in particular for chains of specific heterocycles such as sequences of directly connected pyridine (py) and pyrimidine (pym) rings, which are known to fold into extended helical structures. Since the hydrazone (hyz) group represents an isomorphic analogue of a py site, the condensation of hydrazine and carboxaldehyde derivatives of pym offers a very efficient approach to strands incorporating hyz instead of py units and constituted by sequences of alternating hyz and pym groups. A series of such strands of different lengths, up to ten hyz units, *i.e.*, **1**–**7**, were synthesized. Their spectral properties indicate that they fold indeed into helical shapes. Extensive characterization was performed in solution by ^{1}H-NMR spectroscopy and in the solid state by determination of the crystal structures of eight such strands. They all display the expected helical geometry with up to $3\,^1/_3$ turns and direct stacking contacts. The efficiency and flexibility of the synthetic approach as well as its wide potential for generation of diversity through lateral decoration make the (hyz–pym) subunit a particularly attractive helicity codon.

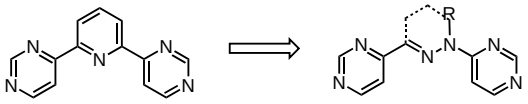
Introduction. – The design of molecular strands capable of taking up defined and predictable shapes is of much interest in view of its relation to biological folding processes in proteins as well as of the access it provides to the generation of well-defined geometries for functional devices and materials. Intense activity has recently been displayed in this area, implementing various types of supramolecular, noncovalent interactions (H-bonding, stacking and electrostatic interactions, metal-ion coordination) as well as medium effects, to induce the self-organization of a molecular strand into specific architectures [1]. A range of geometries from entirely helical to fully linear may thus be targetted.

In our laboratories, we have made use of different interaction patterns and structuration subunits to generate single helices [2–8] and double helices [8a][9–11] as well as extended linear chains [12]. In particular, we have shown that specific sets of connected heterocyclic rings such as pyridine–pyrimidine (py–pym) [2–4], pyridine–pyridazine [5], or naphthyridine–pyrimidine [6] units represent *helicity codons* that enforce the helical wrapping of polyheterocyclic strands. In addition to their static structural features, such strands present, by virtue of the potential coordination sites they possess, dynamic functional features as demonstrated by the extension/contraction motional processes resulting from the reversible interconversion between helical and linear states triggered by metal-ion binding [12][13]. Furthermore, various other

functional properties may be accessible through the precise positioning of photoactive, electroactive, *etc.*, groups, made possible by folding control.

In view of this rich palette of features, an efficient synthetic access to shape-programmed molecular strands is highly desirable. We present here a general scheme to achieve this goal together with extensive structural characterization of the resulting compounds through X-ray crystallography.

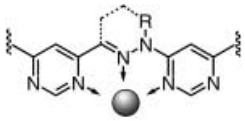
Synthetic and Structural Principles. – For the helical strands based on py–pym sequences previously synthesized in our laboratory [2–4], we made use of a well-defined but laborious synthetic procedure for building up such chains of directly connected heterocycles. The isomorphic correspondence between a 2,6-disubstituted pyridine ring (see **A**) and a hydrazone (hyz) group (see **A′**) provides a solution for greatly facilitating the synthetic procedure by replacing the formation of inter-heterocyclic C–C connections by hydrazone condensation [7].



A **A′**

Generalizing this earlier work, a strand consisting of a sequence of repeating hydrazone–pyrimidine (hyz–pym) units is expected to undergo enforced self-organization into a helical shape. Thus, the hyz–pym group is a *helicity codon* isomorphic to the py–pym one. We describe here the synthesis and structural characterization, both in solution (by NMR spectroscopy) and in the solid state (by X-ray crystallography), of a series of molecular strands of various lengths, *i.e.*, of **1**–**7**, implementing the hyz–pym subunit.

Some general considerations concerning the construction of the ligands were taken into account for planning the synthetic procedures. First, one helical turn is constituted of three hyz–pym units. A sequence pym–hyz–pym corresponds to a tridentate coordination site so that a hydrazone unit is associated with a coordination site (see **B**). On the other hand, a strand containing 4, 6, 8, or 10 hyz groups should be a molecular helix presenting, respectively $1^1/_3$, 2, $2^2/_3$, and $3^1/_3$ turns.

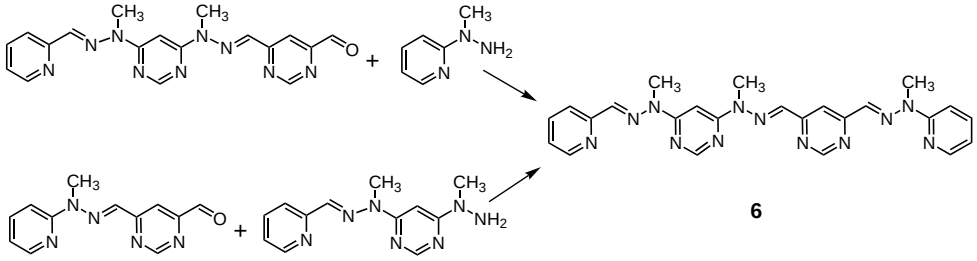


B

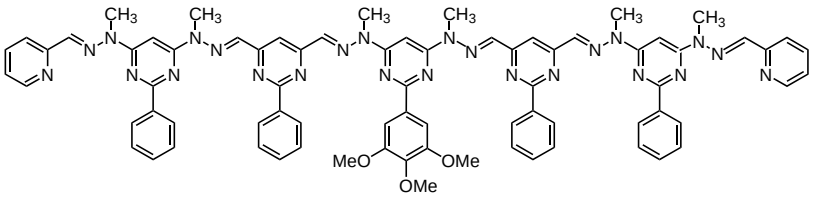
Second, the isomorphic correspondence between a 2,6-disubstituted pyridine and a hydrazone group allows the synthetic connection at this site and, thus, the use of simple pyrimidine building blocks for generating the helical strand. Consequently, the synthesis is greatly facilitated and presents more flexibility as well as wider potential. A strand having an even number of hydrazone functions may be prepared *via* a route involving a desymmetrization step followed by a symmetrical double-chain extension, a

methodology used in natural-product synthesis [14]. In the case of an odd number of hyz groups, the double-chain extension is not possible, but, due to the flexibility of the synthetic pathway, a ligand of this type could be easily synthesized. For example, the 3-sites strand **6** was obtained following two pathways (*Scheme 1*). Both linear (building-blocks stringing) and convergent synthetic pathways may be followed.

Scheme 1



6



3e

The broader potential of the synthesis results from the use of simple and easily functionalizable building blocks giving access to numerous combinations as illustrated by compound **3e** where differently substituted hyz and pym groups are combined, bearing diverse groups at both the pym and the hyz units.

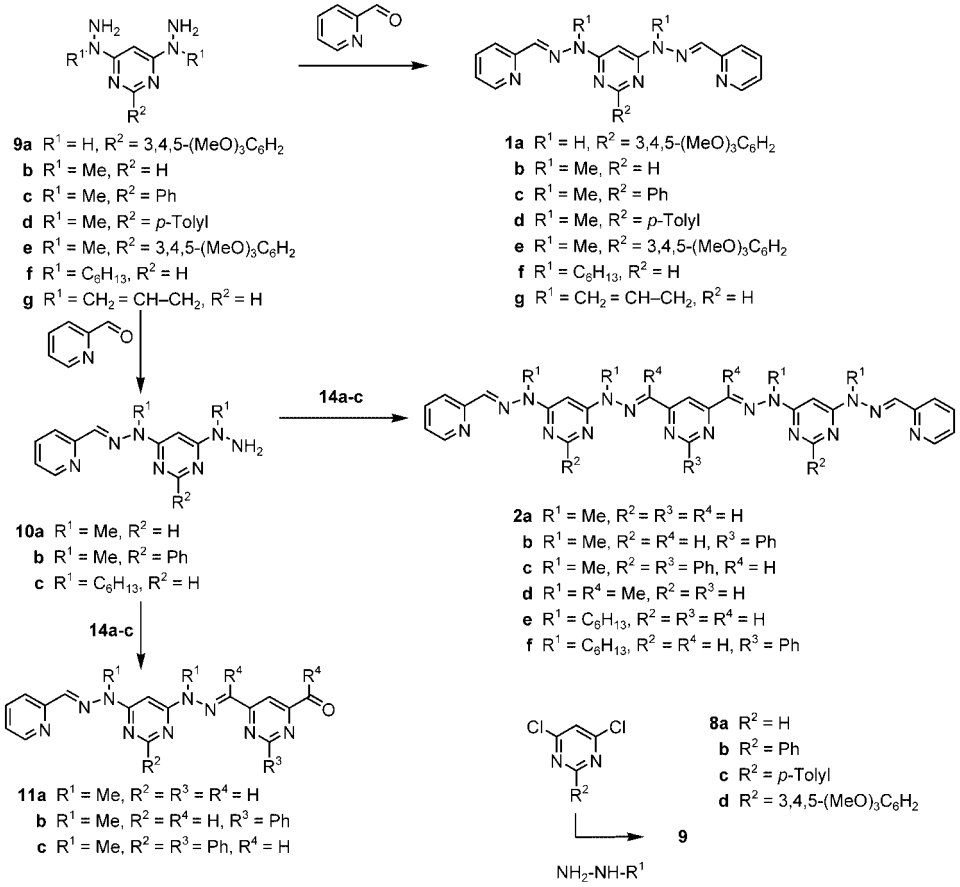
It is, thus, possible to use the ternary hydrazone N-atom, in addition to the 2 position of the pym ring, for 'decorating' the strand by grafting lateral groups possessing specific properties. This is in particular of interest for modulating the solubility in different media. For instance, to increase the solubility in organic solvents, one may use as starting material *N*-alkylhydrazine groups or a pyrimidine ring bearing a trimethoxyphenyl substituent at C(2). The introduction of lateral residues bearing functional groups such as allyl, hydroxyethyl (by using *N*-allyl- or *N*-(hydroxyethyl)-hydrazine) makes possible further functionalization of the strands.

The replacement of a 2,6-disubstituted pyridine ring by a hydrazone group also confers more flexibility to the hyz–pym strand due to the greater conformational mobility of the hyz unit.

Finally, the condensation of a 4,6-dihydrazinopyrimidine with a pyrimidine-4,6-dicarboxaldehyde gives access to helical polymers, thus extending the procedure towards the preparation of novel materials [15].

Synthesis of Strands 1–7. – For the synthesis of the strands **1**–**5** and **7** having an even number of sites, a chain-doubling strategy was used. In this case, the aldehyde or hydrazine precursor chain was constructed in a linear manner by a procedure of repetitive condensation-disymmetrization of the starting pyrimidine-dicarboxaldehyde or dihydrazinopyrimidine (yields of 20–80%), and the final strand was obtained by symmetric double condensation of this precursor with either a dialdehyde or a dihydrazine (yields of 8–75%) (*Schemes 2* and *4*). The 2-sites chain **1** was obtained by condensation of a 4,6-dihydrazinopyrimidine **9** (synthesized from **8**, see *Scheme 2*) with pyridine-2-carboxaldehyde[1]).

Scheme 2. *Synthesis of the 2- and 4-Sites Strands* **1** *and* **2** *and of the Precursors* **11** (uncoiled representation)



For the longer strands **2**–**5**, a disymmetrization procedure was required to progressively build up the components. The synthesis may be conducted along two different pathways, which lead to reverse positioning of the hydrazone functions along the final chains. They involve the use of either pyridine-2-carboxaldehyde to

[1]) Compound **1c** was first synthesized by *George Blasen*.

desymmetrize a 4,6-dihydrazinopyrimidine (in 1:1 stoichiometry; *Schemes 2* and *3*) or 2-hydrazinopyridine to desymmetrize pyrimidine-4,6-dicarboxaldehyde (in 1:1 stoichiometry; see *Scheme 4*). This strategy was successfully employed for preparing the 4-sites strands **2** (from **9** *via* **10**, see *Scheme 2*) and their analog **7** (from **14a** *via* **15**, see *Scheme 4*). During the first desymmetrization step involving the condensation of 1 equiv. of pyridine derivative (pyridine-2-carboxaldehyde or a 2-hydrazinopyridine **26**) and 1 equiv. of a pyrimidine derivative (**9** or **14a**,**b**, resp.) in EtOH, the precursors **10** or **15** could not be obtained pure, but were contaminated by the dihydrazone of type **1**. Increasing the amount of pyrimidine derivative (2, 3, or 4 equiv. of pyrimidine-dicarboxaldehyde **14a**,**b** to 1 equiv. of hydrazinopyridine derivative) and working at low temperature, did not preclude the formation of the corresponding 2-sites compounds due to the high reactivity of the aldehyde. Purification by flash chromatography (FC; alumina or silica gel) was necessary to obtain the precursors **10** (40–80% yield) and **15** (30–40% yield). A possible alternative could be the generation of ketone precursors, by using the diketone **14c**, in view of the lower reactivity of ketones compared to the aldehydes. On the other hand, this nonselectivity was useful, since it generated in one step both the 2-sites compounds **1** and the precursors **10** and **15** of the 4-sites strands.

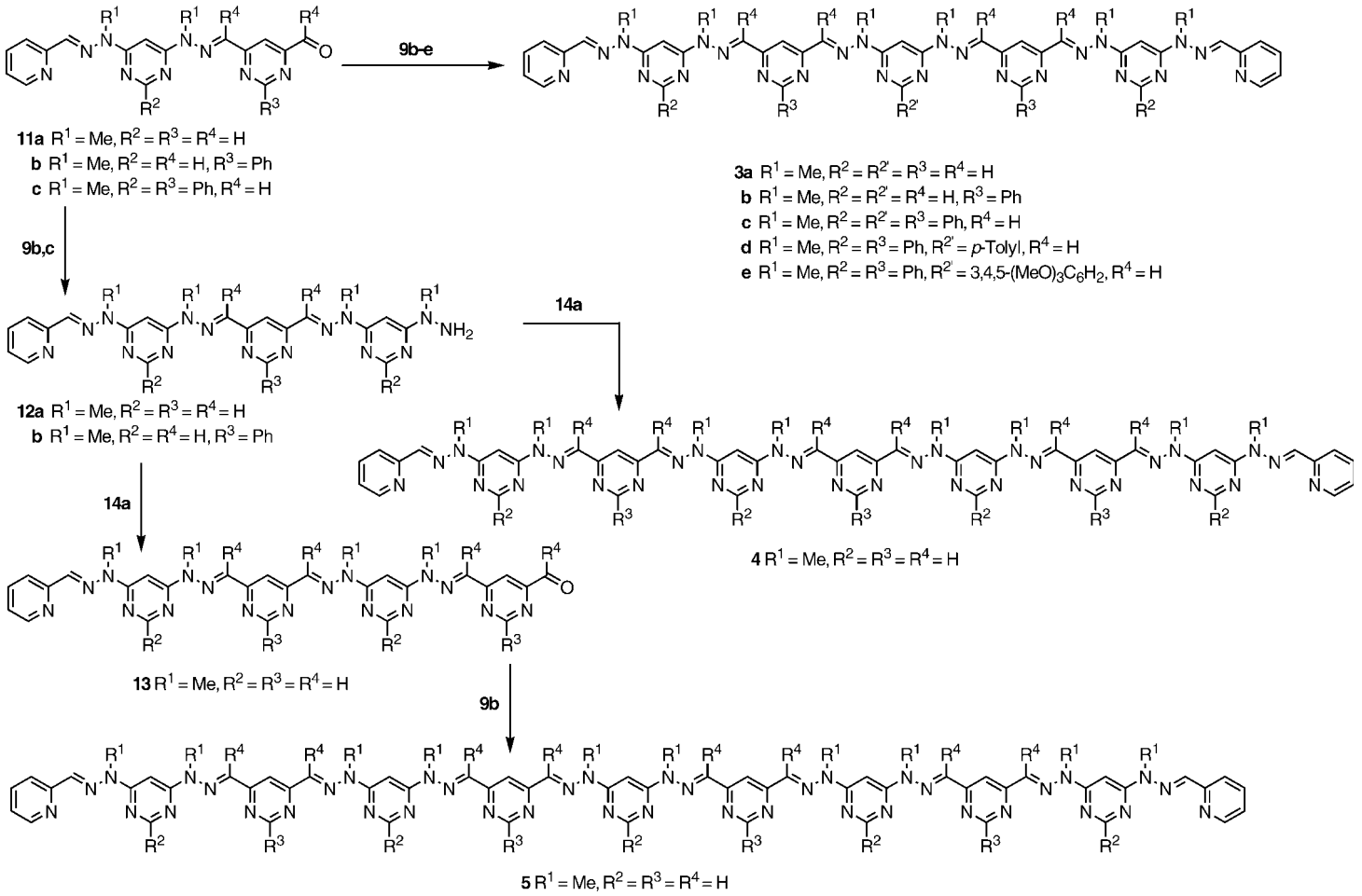
It was noted that the reactions involving *N*-hexylhydrazine derivatives were faster than those with hydrazine or methylhydrazine derivatives. Furthermore, the two dialdehydes **14a** and **14b** (*Scheme 5*) showed different reactivities due to the presence of the phenyl ring, **14a** being much more reactive than **14b**.

Interestingly, the reactivity of the precursor components decreased with increasing chain length. For example, to obtain **13**, it was necessary to heat **12a** (1 equiv.; obtained from **11a**) and dialdehyde **14a** (2 equiv.) to 40–45° during several hours (*Scheme 3*). Similarly, prolonged heating (*ca.* 50 h under reflux) was required in the case of the preparation of the 10-sites strand **5** by the double condensation of aldehyde **13** with dihydrazine **9b** in EtOH/$CHCl_3$ 3:1 (*Scheme 3*). This decrease in reactivity may result from a combination of steric and electronic effects: a longer chain corresponds to an increase in helical turns, which may hinder the approach towards the reaction centers; on the other hand, the helical structure involving π-π stacking of the quasi-superimposed pyrimidine rings may modify the electronic structure of the molecule and influence the reactivity.

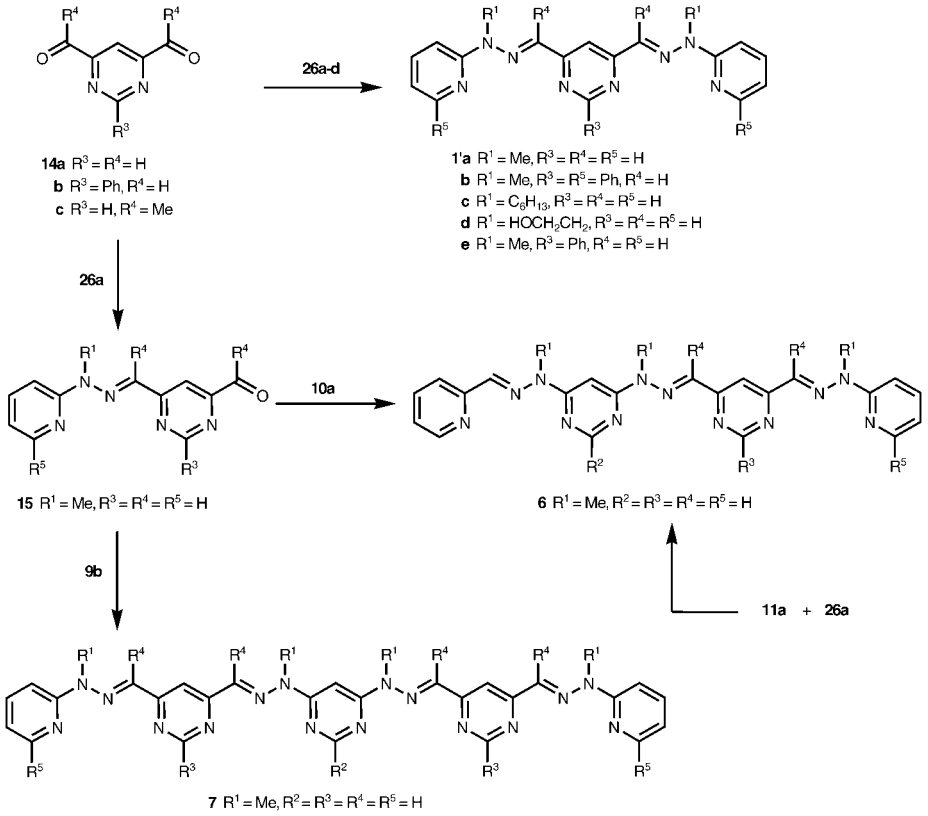
The reaction of the hydrazone-type precursor **10a** (1 equiv.) with 1–4 equiv. of dialdehyde **14a** at room temperature in EtOH yielded a mixture containing excess dialdehyde **14a**, monoaldehyde precursor **11a**, and the 4-sites entity **2a** (*Scheme 2*). The latter was not soluble in EtOH and precipitated; filtering and washing with EtOH gave a filtrate containing **11a** and **14a**. The monoaldehyde **11a** was soluble in EtOH but not in MeCN, while the dialdehyde **16a** was soluble in MeCN, which allowed isolation of **11a** in satisfactory purity by precipitation with MeCN from its EtOH solution. A similar procedure was used to obtain the precursor hydrazine **12a** and aldehyde **13**. Due to the decrease in reactivity with increasing chain length noted above, the reaction of **12** and **13** may be controlled by means of the stoichiometry (dialdehyde or dihydrazine in excess) and the temperature (heating to 40–50°).

The 3-sites species **6** presenting mixed hydrazone positioning was prepared from **14a** *via* **15** as shown in *Scheme 4*. The methyl-bearing 4-sites species **2d** was obtained by

Scheme 3. *Synthesis of the 6-, 8-, and 10-Sites Strands* **3**–**5** (uncoiled representation)



Scheme 4. *Synthesis of the 2- and 4-Sites Strands* **1′** *and* **7** *Starting from 2-Hydrazinopyridine and of the 3-Sites Strand* **6** (uncoiled representation)



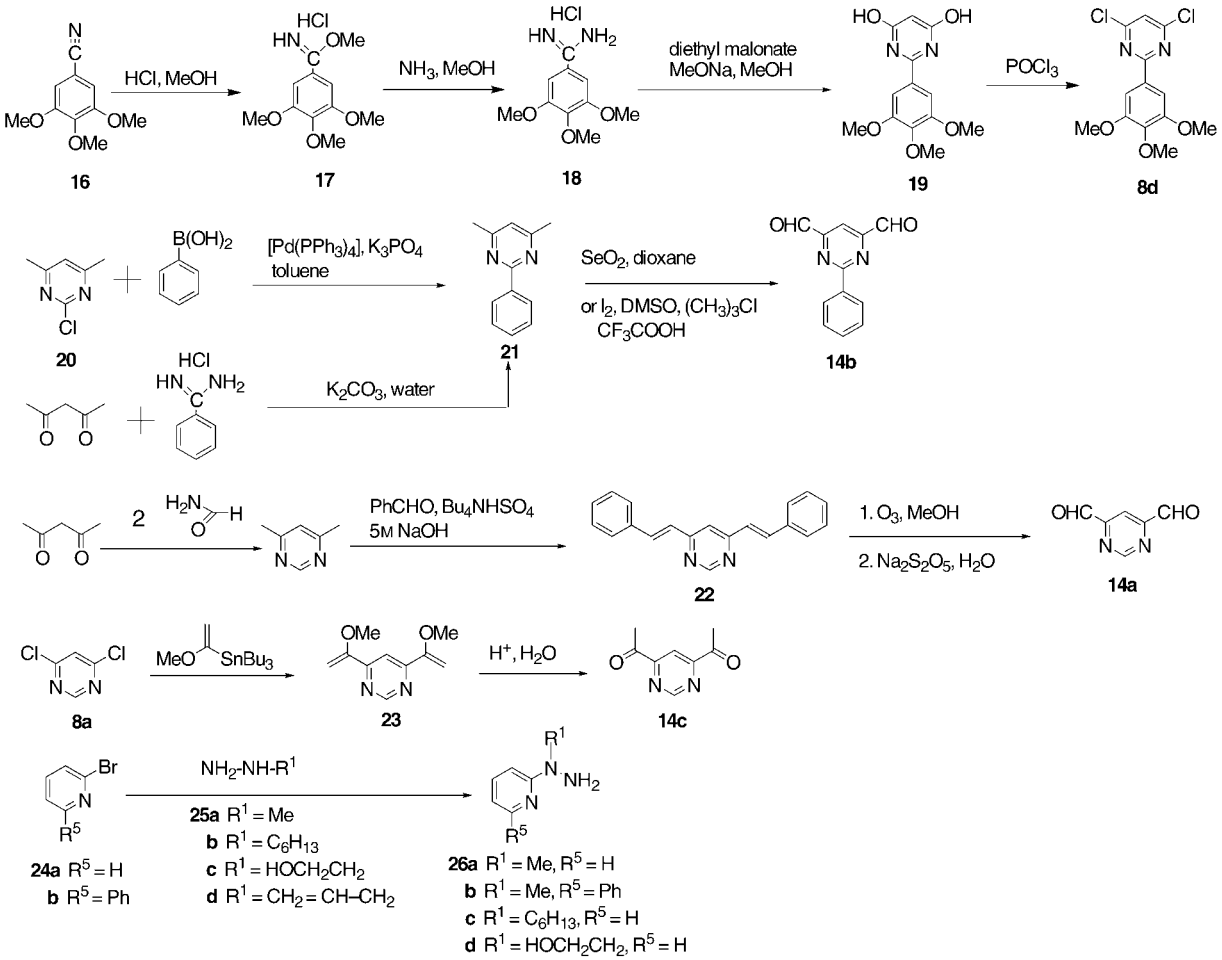
double condensation of 1,1′-(pyrimidine-4,6-diyl)bis[ethanone] (**14c**) [3] with the precursor **10a** (*Scheme 2*).

The preparation of the starting building blocks **8d** and **14**–**26** is summarized in *Scheme 5*.

All compounds gave mass spectroscopic and microanalytical data in agreement with their structures.

Spectroscopic Properties of the Strands 1–7. – *IR Spectra*. The IR spectra agree with the primary structure of the strand **1**–**7**. The absorption bands arising from C–H stretching vibrations (medium intensity) were found between 3000 and 2840 cm^{-1} with asymmetrical ($\tilde{\nu}_{as}(CH_3)$ 2970–2940 cm^{-1}) and symmetrical stretching modes ($\tilde{\nu}_{s}(CH_3)$ 2880–2865 cm^{-1}). In the case of the compounds containing hexyl or hydroxyethyl substituents, the methylene asymmetrical ($\tilde{\nu}_{as}(CH_2)$ 2925–2920 cm^{-1}) and symmetrical stretching bands ($\tilde{\nu}_{s}(CH_2)$ 2855–2920 cm^{-1}) were observed. The OH derivatives (primary alcohols) displayed bands corresponding to the O–H stretching vibrations ($\tilde{\nu}$(OH) 3427 cm^{-1}) and the C–O stretching vibrations ($\tilde{\nu}$(C–O) 980 cm^{-1}). The strong

Scheme 5. *Synthesis of the Heterocyclic Building Blocks*



absorption bands between 1580 and 1594 cm^{-1}, and 1420 and 1480 cm^{-1}, respectively, correspond to the stretching vibration of the C=N hydrazone bond and to the pyrimidine- or pyridine-ring stretching vibrations (skeletal bands).

UV/VIS Spectra. The UV/VIS spectra of **1**–**7** in CH_2Cl_2 display two absorption regions. The first one lies between 225 and 235 nm and corresponds mainly to a π-π transition characteristic of the conjugate C=N groups (hydrazones). The second region ranges from 270 to 380 nm and contains two or three absorption maxima arising mainly from the π-π* transitions of the pyridine and the pyrimidine rings.

The comparison of the UV/VIS spectra of compounds **1**–**7** shows two general trends. First, a hyperchromic effect is observed for the compounds presenting π-π stacking only within the helical chain. This is the case for compounds having no aromatic-ring substituent at C(2) of the pyrimidine ring, or those in which such substituents are not superimposable. The absorption coefficient ε increases when the number of turns of the helical strands increases, ranging, *e.g.*, from 34000–50000 M^{-1} cm^{-1} (for a $^2/_3$ turn strand) to 150000–160000 M^{-1} cm^{-1} for a strand of *ca.* 3 turns. This trend agrees with that observed in the case of the py–pym strands previously studied in our laboratory [4]. However, the ε values are lower in the present compounds, due probably to a decrease in conjugation resulting from the replacement of the pyridine ring by a hydrazone group.

When the helical strand presents superimposed lateral phenyl substituents, generating a supplementary or 'secondary' π-π stacking, a hypochromic effect is observed, as is the case for compounds **2c** ($\varepsilon = 83000 M^{-1}$ cm^{-1}), a $1^1/_3$-turn strand, and **3c** ($\varepsilon = 44800 M^{-1}$ cm^{-1}), a 2-turns strand.

These trends may be understood by taking into account the fact that two factors may affect the molar extinction coefficient ε: the conjugation length increasing the ε value, and the π-π stacking decreasing the ε value (as for base-pair stacking in the DNA double helix).

The analysis of the X-ray structures of the present strands (see below) shows that the stacking within the helices having no superimposed lateral groups is not a perfect one, so that the increase in conjugation with strand length has a stronger effect than the π-π stacking, resulting in an increase in absorption intensity. On the other hand, when lateral phenyl groups able to generate secondary stacking are present, the conjugation effect becomes less important than the π-π stacking so that ε decreases due to the stacking, a hypochromic effect similar to that observed for DNA hybridization.

The second trend observed is a blue shift (a hypsochromic effect) that occurs when the number of turns increases, as in the case of the ligands bearing no lateral phenyl group. This effect may be rationalized by noting that, in the crystal structures of the strands, the primary stacking of the pyrimidine rings is not perfect and is worse in the longer molecules (3 turns) than in the shorter ones (1 or 2 turns). The weak bathochromic effect observed in the case of the ligands presenting 'secondary' stacking between the decorating phenyl substituents may be due to the fact that this lateral stacking stabilizes the primary one and becomes stronger as the number of phenyl groups increases.

The red shift observed in some cases may be assigned to the presence of a more extensively conjugated pyrimidinedicarboxaldehyde dihydrazone, unit, which also increases the absorption; thus, **1′a** has a λ_{max} higher than that of **1b**, and **7** (containing

two dicarboxaldehyde dihydrazone units) has λ_{max} 331 nm, while **2a** (containing only one dicarboxaldehyde dihydrazone unit) has λ_{max} 316 nm.

^{1}H-NMR Spectroscopy. The ^{1}H-NMR data provide clear indications of the helical shape of the strands **1**–**7** in solution. One of the characteristic features of all the helical py–pym oligomers previously reported [2–4] is the upfield shift in the ^{1}H-NMR spectrum of the terminal pyridine protons in the helical structure, resulting from the shielding effect due the aromatic heterocyclic rings positioned above the terminal pyridine ring. In the present case, the signal of H–C(4) of the terminal pyridine shows a shift from δ 8.18 for **11b**, which does not form a helical turn, to δ 7.13 for **2c**, where the proton is shielded by the aromatic rings lying above. The same behavior is observed for **3c** with an increase in 0.2 ppm in the upfield shift probably resulting from the increase in the number of stacked rings. Such a cumulative effect was already observed in the helical structures composed of py–pym sequences possessing from 1 to 4 turns [2–4] and in 1- and 2-turns helices incorporating two hydrazone fragments [7]. A comparison of the ^{1}H-NMR shifts of the terminal pyridine protons for different strands is given in the *Table*. Similar remarks concern the pyrimidine-ring protons, which also display a progressive upfield shift with the increase of the number of turns.

Table 1. *^{1}H-NMR Chemical Shifts of the Four Protons of the Terminal Pyridine Rings of Different Strands*

Strand	Number of turns	Chemical shifts [ppm]			
		H–C(3)	H–C(4)	H–C(5)	H–C(6)
1b	$^2/_3$	8.13	7.68	7.23	8.58
2a	$1^1/_3$	7.72	7.13	6.91	8.29
3a	2	7.47	6.97	6.78	8.18
4	$2^2/_3$	7.42	6.86	6.73	8.13
5	$3^1/_3$	7.33	6.83	6.72	8.13

The most-revealing features confirming the helical structure of strands **1**–**7** are provided by the 2D NMR nuclear *Overhauser* effect (NOE) data obtained from NOESY and ROESY experiments, which indicate correlations due to the spatial proximity of the protons. Distinct NOE effects are observed between the protons oriented towards the interior of the helix, *e.g.*, between the pyrimidine protons at C(5) of the ring and the proton at C(2) of the pyrimidine ring. The intensity of the correlation trace is in line with the distance between the protons, as observed in the crystal structure: the relative intensity of the trace decreases as the distance increases. As an example, the NOESY trace of the aromatic domain of the 10-turns strand is shown in *Fig. 1*.

Crystal Structures of Eight hyz–pym Strands. – An extensive radiocrystallographic investigation was performed with several of the synthesized hyz–pym strands to specify their solid-state structures and to correlate them with the data provided by NMR spectroscopy in solution. Single crystals suitable for X-ray crystallography were obtained by diffusion of a nonsolvent (MeCN, MeOH, heptane, Et_2O, $^iPr_2O$, EtOH) into a CH_2Cl_2 or $CHCl_3$ solution of the strands **1c**, **2a**, **2c**, **3a**, **3c**, or **5**–**7** at room temperature in a glass tube. Of these eight strands, five have no phenyl group attached

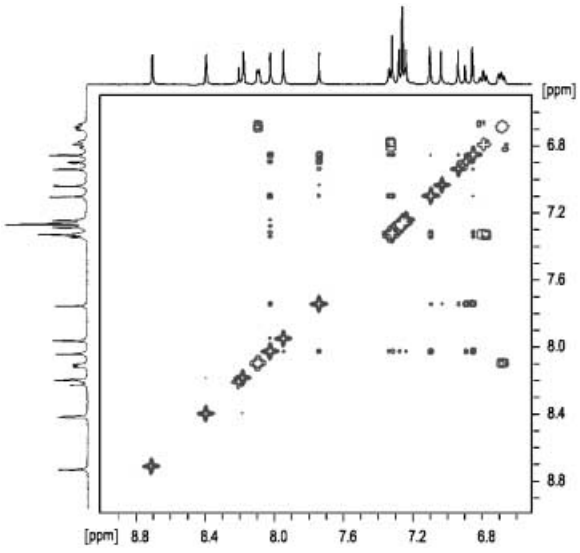


Fig. 1. *Nuclear*-Overhauser-*effect* (NOE) *correlations for the 10-hydrazone-sites strand* **5** *in the 6.5–9 ppm region* (NOESY experiment on a *Bruker-300-MHz* spectrometer)

to the pyrimidines (**2a**, **3a**, and **5**–**7**) and three bear phenyl groups at C(2) of the pyrimidine ring (**1c**, **2c**, and **3c**). The crystal structures of all eight strands (see *Figs. 2–5*) confirm their helical shape (as shown in *Fig. 6* for **5**) and suggest that the polymeric strands obtained by polycondensation of a pyrimidinedicarboxaldehyde with a dihydrazinopyrimidine have also a helical shape [15].

In all cases, the unit-cell contains an even number of molecules (Z), corresponding to $Z/2$ enantiomer pairs so that the crystal is achiral (compounds (Z molecules/unit): **5** (2), **3a** (4), **3c** (2), **2a** (8), **7** (2), **2c** (8), **6** (2), **1c** (8)). The same feature was observed for the hydrazone-containing strands investigated earlier [7], whereas, in the case of the py–pym strands, chiral channels were generated in the solid-state assembly from the achiral linear strands [4].

The *N*-methyl substituted N-sites are practically planar due to conjugation with the pyrimidine ring and the hydrazone bond. The torsional angles between the plane defined by the hydrazone group and the pyrimidine ring are between 5 and 15° and may be as small as 0.2–3°, whereas the related angles in the py–pym based helices lie around 10–14° [4]. This may result from the higher flexibility of the present strands due to the replacement of the pyridine ring by a hydrazone group.

The internal void of the helices is *ca.* 1.1–1.5 Å in diameter, as compared to 2 Å in the pym–py helices (considering a projection in a plane and taking into account the *Van der Waals* radii of diagonally located N and C–H sites). The N-atoms lining the internal void might serve as coordination sites for metal ions in a potential ion-channel fashion. On the other hand, these helical strands represent coiled molecular wires of nanometric length (30–80 Å), which may be switched into a linear wire by coordination of suitable metal ions (Pb^{2+}, Zn^{2+}, *etc.*); this is the case for the py–pym strands [13] as well as for the present hydrazone strands [12].

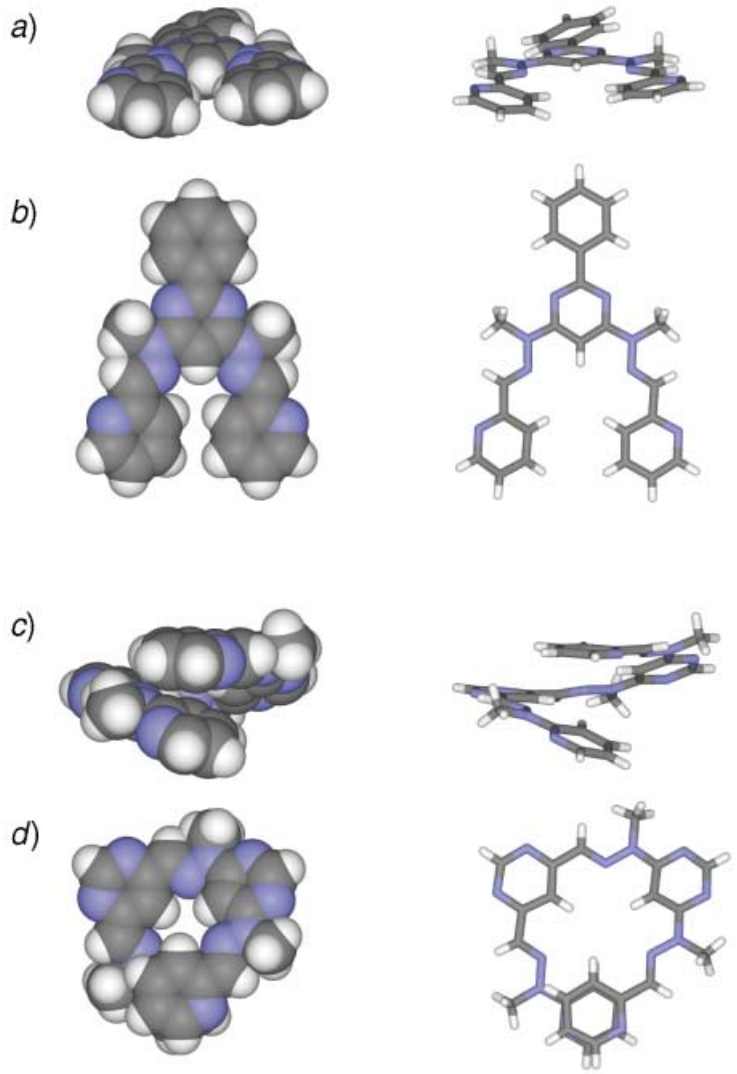


Fig. 2. *Crystal structures of* a) b) *strand* **1c** *and* c) d) *strand* **6**. Stick (right) and space-filling (left) representations; *a*) *c*) side views and *b*) *d*) axial views.

The helical pitch of the helices lies between 3.50–3.70 Å, depending on the presence or absence of lateral phenyl groups. The heights of these molecular coils range from 3.50 (**2**) to 11.60 Å (**5**).

The crystals contain some solvent molecules (as also indicated by elemental analysis), but these molecules are too large for inclusion into the internal void of the helices or do not have interactions that could lead to such inclusion.

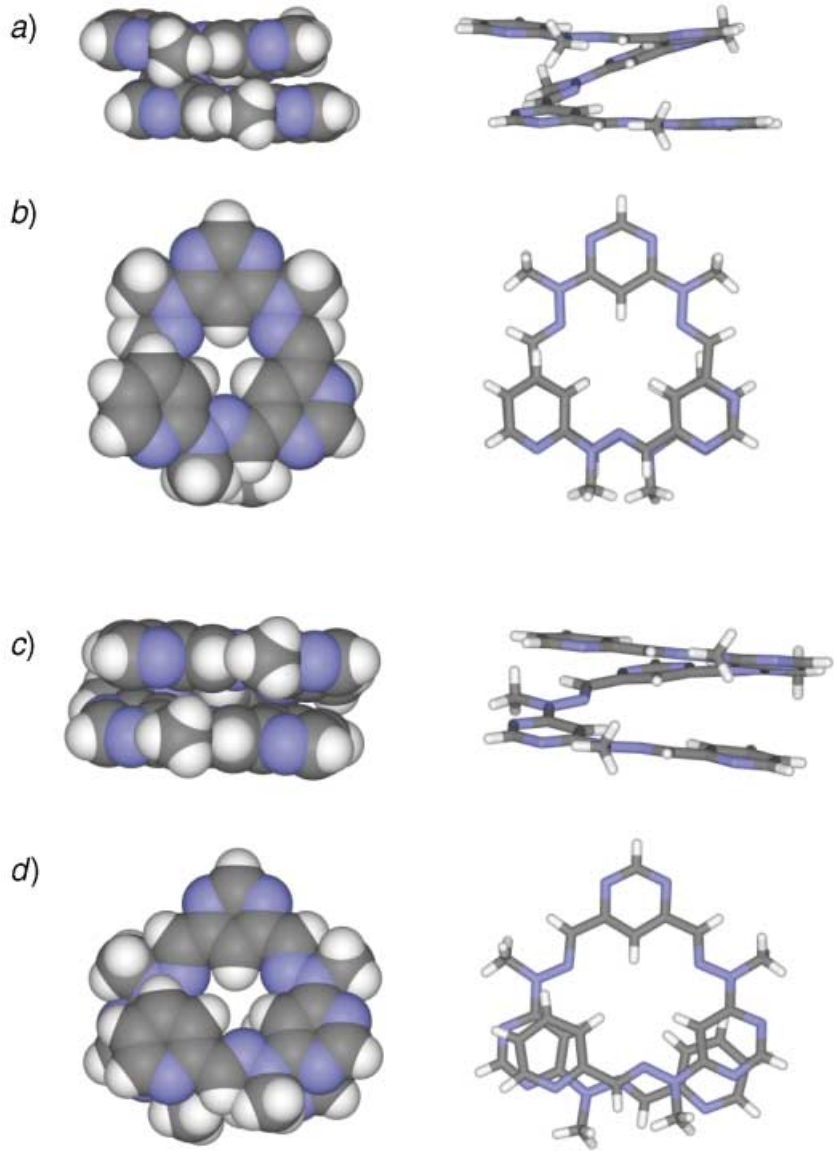


Fig. 3. *Crystal structures of* a) b) *strand* **7** *and* c) d) *strand* **2a**. Stick (right) and space-filling (left) representations; *a*) *c*) side views and *b*) *d*) axial views.

The strands bearing a phenyl group generate more-regular helices with better overlap of the pym rings, due probably to the additional stacking provided by the lateral phenyl groups. Conversely, the strands without phenyl groups present imperfect pym stacking and a somewhat deformed helical structure; the stacking of the pyrimidine rings becomes worse as the strand length increases. Thus, a comparison of the axial view

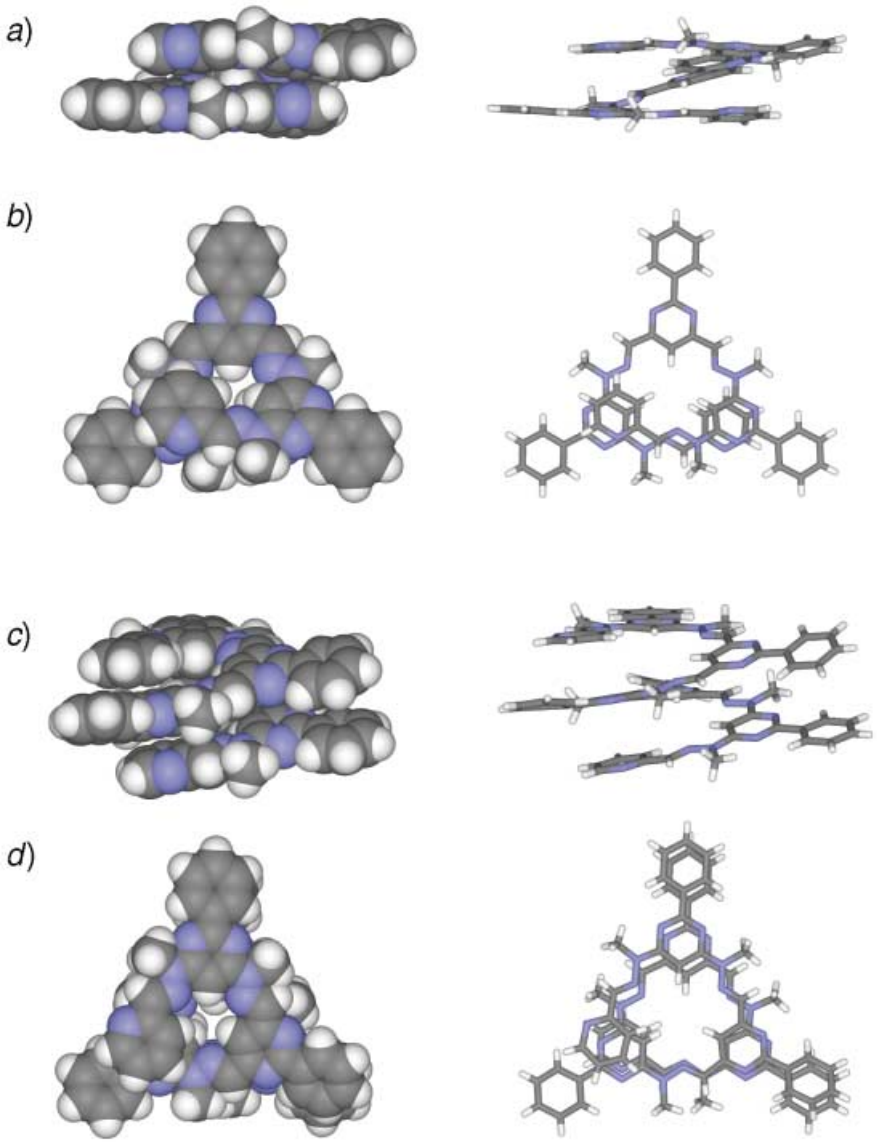


Fig. 4. *Crystal structures of* a) b) *strand* **2c** *and* c) d) *strand* **3c**. Stick (right) and space-filling (left) representations; *a*) *c*) side views and *b*) *d*) axial views.

for the $1^1/_3$-turn strand **2a** (*Fig. 3*,*d*) and for the 2-turns strand **3a** (*Fig. 5*,*b*) (having no decorating phenyl) with the corresponding strands **2c** (*Fig. 4*,*b*) and **3c** (*Fig. 4*,*d*), (having a phenyl at C(2) of each pyrimidine unit), respectively, shows that the stacking is better and the helix is more regular for the second ones. One may note that energy-minimization computations (SPARTAN program, AM 1 force field) gave structures for **2c** and **3c** very close to those determined by X-ray crystallography.

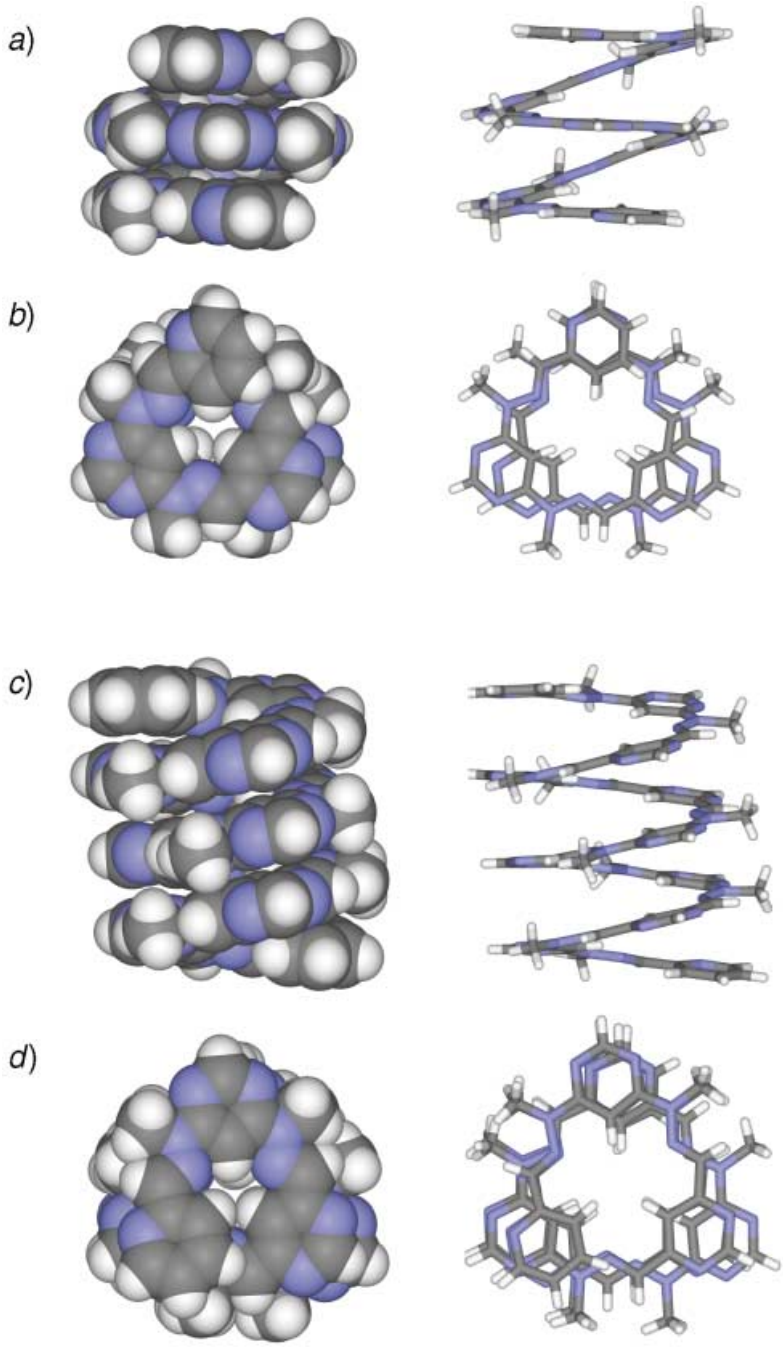


Fig. 5. *Crystal structures of* a) b) *strand* **3a** *and* c) d) *strand* **5**. Stick (right) and space-filling (left) representations; *a*) *c*) side views and *b*) *c*) axial views.

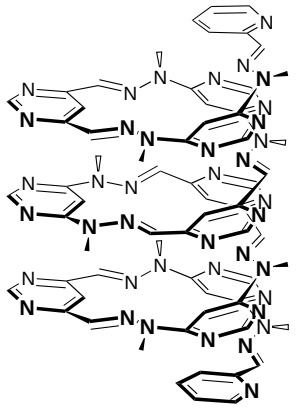


Fig. 6. *Structural formula of the helical strand* **5**

The effect of conjugated units may be seen by comparing the structure of the strand **2a** (containing only one central pyrimidinedicarboxaldehyde-derived unit; *Fig. 3*,*c* and *d*) with that of **7** (*Fig. 3*,*a* and *b*), which incorporates two pyrimidinedicarboxaldehyde-derived units and presents, thus, more-extensive conjugation. The better stacking in the second strand is reflected in a slow decrease in absorption coefficient ε (from 68100 to 67000) and a red shift (from 316 to 330 nm) due to more-extensive conjugation.

Conclusions. – The results described here indicate that the hydrazone route provides a very efficient approach to molecular chains constituted of extended hyz–pym sequences. Such strands are programmed to undergo folding into helical shapes. The synthetic pathway offers great flexibility and presents wide potential for the generation of structural diversity through the introduction, on both the pym and the hyz sites, of various lateral groups decorating the exterior of the helix. These features make the hyz–pym subunit a particularly attractive helicity codon for the exploration of numerous structural and functional variations.

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Experimental Part

General. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Allylhydrazine (**25d**) [16] and hexylhydrazine (**25b**) [17] were prepared from the corresponding bromides and hydrazine. The (2-hydroxyethyl)hydrazine (=2-hydrazinoethanol; **25c**) was prepared as described [18] or purchased from *Sigma-Aldrich*. Pyrimidine-4,6-dicarboxaldehyde (**14a**), first prepared by ozonolysis of **22** [19a,b], was also obtained here by ozonolysis of **22**, but by using the same procedure as described for the preparation of pyridazine-3,6-dicarboxaldehyde [19c] without purification by sublimation under high vacuum, the yield being 30–40%. Dicarboxaldehyde **14a** is an unstable, air-sensitive

compound and was stored under Ar at low temp. (in a freezer). The 4,6-distyrylpyrimidine (**22**) was synthesized by the condensation of benzaldehyde with 4,6-dimethylpyrimidine [20], the latter being obtained from acetylacetone and formamide, as described [21]. The 2-phenylpyrimidine-4,6-dicarboxaldehyde (**14b**) was prepared by oxidation of 4,6-dimethyl-2-phenylpyrimidine (**21**) with selenium dioxide [22] or with I_2/^{t}BuI in DMSO [23] as described for other heterocyclic dimethyl derivatives [23a]; **21** was prepared from acetylacetone and benzamidine hydrochloride (= benzenecarboximidamide hydrochloride), as described [24], or by a new method, reported below. The 1,1′-(pyrimidine-4,6-diyl)bis[ethanone] (**14c**) was prepared by the coupling of (1-methoxyethenyl)tributylstannane [25] with 4,6-dichloropyrimidine (**8a**), followed by acid hydrolysis of the methoxyvinyl groups of **23** [3b][26]. The 4,6-dichloro-2-(*p*-tolyl)pyrimidine (**8c**) was prepared from 2-(*p*-tolyl)pyrimidine-4,6-diol [27] by treatment with $POCl_3$, as described [28]. The 2-(1-methylhydrazino)pyridine (**26a**) was prepared from 2-bromopyridine (**24a**) and methylhydrazine (**25a**), as described [29]. The 2-bromo-6-phenylpyridine (**24b**) was synthesized by using a *Grignard* reagent, as described [30]. All org. solns. were routinely dried (Na_2SO_4) and evaporated in a rotary evaporator. TLC: *Polygram Alox N/UV$_{254}$* precoated plastic sheets or *Polygram Sil-G/UV$_{254}$* precoated plastic sheets. Prep. TLC: 20 × 20-cm plates covered by aluminium oxide *60 F$_{254}$* (1.5 mm) from *Merck*. Flash chromatography (FC): 230–400 mesh silica-gel particles or neutral alumina (act. 2) from *Merck*. M.p.: *Büchi B-540* melting-point apparatus; uncorrected. UV/VIS Spectra: *Varian-Cary-3* spectrometer; λ_{max} in nm, ε in M^{-1} cm^{-1}. IR Spectra: *Perkin-Elmer 1600* – FTIR spectrometer; KBr pellets; in cm^{-1}. ^{1}H-NMR (200, 300, 400, or 500 MHz), ^{13}C-NMR (50, 75, 100, or 125 MHz), and 2D-NMR Spectra: *Bruker AC-200*, *Avance-300*, *Avance-400*, or *Avance-500* spectrometers, resp.; $CDCl_3$ as solvent, unless otherwise noted; chemical shifts δ in ppm with a residual solvent proton peak as ref.; 2D-NMR experiments were: COSY (correlation spectroscopy), HMBC (heteronuclear multiple-bond correlation), HMQC (heteronuclear multiple-quantum correlation (coherence)), NOESY (nuclear *Overhauser* enhancement spectroscopy or nuclear *Overhauser* and exchange spectroscopy), ROESY (rotating-frame *Overhauser* enhancement (effect) spectroscopy). Electron-ionization (EI), fast-atom-bombardment (FAB) MS, matrix-assisted laser-desorption (MALDI) MS, and low- or high-resolution (HR) MS were carried out by the Service d'Analyse de l'Université Louis Pasteur, in *m*/*z* (rel. %). Microanalyses were performed by the Service Central de Microanalyse du CNRS, Faculté de Chimie, Strasbourg or at FZK, Karlsruhe.

Pyridine-2-carboxaldehyde [2-(3,4,5-Trimethoxyphenyl)pyrimidine-4,6-diyl]dihydrazone (**1a**). A soln. of 4,6-hydrazino-2-(3,4,5-trimethoxyphenyl)pyrimidine (**9a**; 15 mg, 0.045 mmol) and pyridine-2-carboxaldehyde (15 mg, 0.140 mmol) in abs. EtOH (5 ml) was stirred at r.t. for 4 h under Ar. The solvent was evaporated and the residue purified by FC (Al_2O_3, $CHCl_3$): **1a** (20 mg, 87%). White solid. M.p. 128°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 10.02 (*s*, 2 H); 7.69 (*d*, 2 H); 7.41 (*s*, 2 H); 7.23 (*d*, 2 H); 7.15 (*t*, 2 H); 6.87 (*s*, 2 H); 6.96 (*s*, 2 H); 6.95 (*d*, 2 H); 6.73 (*t*, 2 H); 6.35 (*s*, 1 H); 3.93 (*s*, 6 H); 3.82 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 162.0; 154.0; 149.9; 142.8; 137.0; 133.0; 124.0; 119.7; 105.0; 81.0; 56.3. MALDI-MS: 485.3 (100, $[M+H]^+$).

Pyridine-2-carboxaldehyde (Pyrimidine-4,6-diyl)dihydrazone (**1b**). A soln. of pyridine-2-carboxaldehyde (40 mg, 0.374 mmol) and **9b** (30 mg, 0.179 mmol) in EtOH (5 ml) was heated to reflux for 3 h. Then, the mixture was cooled, concentrated under vacuum and filtered. The precipitate was washed with EtOH and dried for 10 h under high vacuum: **1b** (38 mg, 61%). White solid. M.p. 246–248° (recryst. from pyridine). UV/VIS ($CHCl_3$): 336.0. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.58 (*d*, 2 H); 8.43 (*s*, 1 H); 8.13 (*d*, 2 H); 7.86–7.81 (*m*, 3 H); 7.68 (*t*, 2 H); 7.23 (*t*, 2 H); 3.64 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 162.7; 156.7; 155.0; 149.4; 136.9; 136.0; 122.9; 119.4; 88.8; 29.6. EI-MS: 346.2 (18, M^+), 268.2 (100, $[M-78]^+$). FAB-MS: 347.3 (100, $[M+H]^+$). HR-FAB-MS: 347.1731 ($[C_{18}H_{18}N_8+H]^+$; calc. 347.1733). Anal. calc. for $C_{18}H_{18}N_8$: C 62.41, H 5.24, N 32.35; found: C 62.21, H 5.01, N 32.21.

Pyridine-2-carboxaldehyde [2-(4-Methylphenyl)pyrimidin-4,6-diyl]dihydrazone (**1d**). As described for **1b**, with pyridine-2-carboxaldehyde (45 mg, 0.421 mmol), **9d** (50 mg, 0.194 mmol), and EtOH (3 ml): **1d** (70 mg, 83%). White solid. M.p. 285–287°. UV/VIS ($CHCl_3$): 300.0 (77900). ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.61 (*d*, 2 H); 8.36 (*d*, 2 H); 8.17 (*d*, 2 H); 7.83 (*s*, 2 H); 7.81 (*s*, 1 H); 7.71 (*td*, 2 H); 7.27 (*d*, 2 H); 7.22 (*td*, 2 H); 3.78 (*s*, 6 H); 2.36 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 163.2; 162.4; 155.6; 149.4; 140.5; 136.4; 136.03; 135.5; 129.0; 128.1; 122.9; 119.5; 86.9; 29.7; 21.5. FAB-MS: 437.1 (100, $[M+H]^+$). HR-FAB-MS: 437.2201 ($[C_{25}H_{24}N_8+H]^+$; calc. 437.2202). Anal. calc. for $C_{25}H_{24}N_8$: C 68.79, H 5.54, N 25.67; found: C 68.55, H 5.28, N 25.52.

Pyridine-2-carboxaldehyde [2-(3,4,5-Trimethoxyphenyl)pyrimidine-4,6-diyl]bis(methylhydrazone) (**1e**). As described for **1a**, with 4,6-bis(1-methylhydrazino)-2-(3,4,5-trimethoxyphenyl)pyrimidine (**9e**; 15 mg, 0.045 mmol), pyridine-2-carboxaldehyde (15 mg, 0.140 mmol), and EtOH (5 ml): **1e** (20 mg, 87%). White solid. M.p. 128°. ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.50 (*d*, 2 H); 7.18 (*d*, 2 H); 6.96 (*s*, 2 H); 6.92 (*s*, 1 H); 6.87 (*s*, 2 H); 6.84 (*t*, 2 H); 6.48 (*t*, 2 H); 4.05 (*s*, 6 H); 3.99 (*s*, 3 H); 3.91 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 183.2; 182.12; 153.0; 149.4; 147.6; 136.7; 136.1; 122.9; 119.5; 115.6; 105.3; 86.9; 56.1; 29.7. EI-MS: 512.3 (100, $[M+H]^+$).

Pyridine-2-carboxaldehyde (Pyrimidine-4,6-diyl)bis(hexylhydrazone) (**1f**). As described for **1b**, with pyridine-2-carboxaldehyde (86 mg, 0.803 mmol), **9f** (100 mg, 0.325 mmol) and EtOH (3 ml). To the mixture concentrated under vacuum (0.5–1 ml), MeCN (2 ml) was added. The precipitate was washed with MeCN and dried for 10 h under high vacuum: **1f** (145 mg, 92%). White solid. M.p. 123–125°. UV/VIS ($CHCl_3$): 319.0 (38900). IR (KBr): 2925*m*, 2853*w*, 1591*s*, 1571*s*, 1542*m*, 1459*s*, 1426*s*, 1335*w*, 1174*m*, 1144*m*, 1099*m*, 981*m*, 909*w*, 771*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.62 (*d*, 2 H); 8.46 (*s*, 1 H); 8.17 (*d*, 2 H); 7.89 (*s*, 2 H); 7.84 (*s*, 1 H); 7.71 (*t*, 2 H); 4.31 (*t*, 4 H); 1.68 (*t*, 4 H); 1.51–1.29 (*m*, 12 H); 0.89 (*t*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.6; 157.0; 155.3; 149.3; 136.1; 135.9; 122.8; 199.4; 88.7; 42.0; 31.6; 26.6; 25.1; 22.6; 13.9. EI-MS: 486.2 (25, M^+), 408.4 (100, $[M-78]^+$). FAB-MS: 487.4 (100, $[M+H]^+$). HR-FAB-MS: 487.3292 ($[C_{28}H_{38}N_8+H]^+$; calc. 487.3298). Anal. calc. for $C_{28}H_{38}N_8$: C 69.10, H 7.87, N 23.03; found: C 68.85, H 7.53, N 22.88.

Pyridine-2-carboxaldehyde (Pyrimidine-4,6-diyl)bis(prop-2-enylhydrazone) (**1g**). As described for **1b**, with pyridine-2-carboxaldehyde (40 mg, 0.374 mmol), **9g** (40 mg, 0.182 mmol), and EtOH (5 ml): **1g** (43 mg, 59%). White solid. M.p. 200–202°. UV/VIS ($CHCl_3$): 315.0 (35000). ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.61 (*d*, 2 H); 8.48 (*s*, 1 H); 8.18 (*d*, 2 H); 7.95 (*s*, 1 H); 7.85 (*s*, 2 H); 7.73 (*t*, 2 H); 7.25 (*t*, 2 H); 5.97–5.79 (*m*, 2 H); 5.22 (*d*, 2 H); 5.04 (*d*, 2 H); 5.01 (*d*, 4 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 162.7; 157.3; 155.1; 149.5; 138.0; 136.1; 130.1; 123.1; 119.6; 117.1; 88.6; 44.9. FAB-MS: 399.1 (100, $[M+H]^+$). HR-FAB-MS: 399.2058 ($[C_{22}H_{22}N_8+H]^+$; calc. 399.2046). Anal. calc. for $C_{22}H_{22}N_8$: C 66.31, H 5.57, N 28.12; found: C 66.15, H 5.22, N 27.85.

Pyrimidine-4,6-dicarboxaldehyde Bis[methyl(pyridin-2-yl)hydrazone] (**1′a**). As described for **1b**, with **26a** (72 mg, 0.563 mmol), **14a** (40 mg, 0.294 mmol), and EtOH (3 ml): **1′a** (45 mg, 44%). Yellowish solid. M.p. 243–245° (dec.). UV/VIS ($CHCl_3$): 337.0 (39700). ^{1}H-NMR ($CDCl_3$, 200 MHz): 9.08 (*s*, 1 H); 8.42 (*s*, 1 H); 8.29 (*d*, 2 H); 7.83 (*d*, 2 H); 7.83–7.64 (*m*, 4 H); 6.92 (*t*, 2 H); 3.73 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 161.6; 158.9; 157.0; 147.1; 137.6; 132.0; 117.0; 110.4; 110.0; 30.0. EI-MS: 346.1 (17, M^+), 134.1 (100). FAB-MS: 347.1 (100, $[M+H]^+$). HR-FAB-MS: 347.1743 ($[C_{18}H_{18}N_8+H]^+$; calc. 347.1733). Anal. calc. for $C_{18}H_{18}N_8$: C 62.41, H 5.24, N 32.35; found: C 62.14, H 4.97, N 32.17.

2-Phenylpyrimidine-4,6-dicarboxaldehyde Bis[methyl(6-phenylpyridin-2-yl)hydrazone] (**1′b**). As described for **1b**, with **26b** (38 mg, 0.191 mmol), **14b** (20 mg, 0.094 mmol), and EtOH (2 ml) for 5 h: **1′b** (46 mg, 85%). Yellowish solid. M.p. 280–282°. UV/VIS ($CHCl_3$): 263.0 (77300). ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.53 (*dd*, 2 H); 8.42 (*s*, 1 H); 8.11 (*d*, 4 H); 7.85 (*d*, 2 H); 7.81 (*s*, 2 H); 7.77 (*t*, 2 H); 7.57–7.40 (*m*, 11 H); 3.91 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.2; 158.7; 157.8; 156.8; 154.7; 139.2; 139.1; 138.4; 132.9; 130.5; 128.9; 128.6; 128.5; 128.2; 126.7; 120.9; 108.8; 29.9. FAB-MS: 575.5 (100, $[M+H]^+$). HR-FAB-MS: 575.2667 ($[C_{36}H_{30}N_8+H]^+$; calc. 575.2672).

Pyrimidine-4,6-dicarboxaldehyde Bis[hexyl(pyridin-2-yl)hydrazone] (**1′c**). As described for **1b**, with **26c** (100 mg, 0.518 mmol), **14a** (35 mg, 0.257 mmol), and EtOH (2 ml). To the mixture concentrated under vacuum (0.5 ml), MeCN (1–2 ml) was added. The precipitate formed after a while was filtered, washed with EtOH, and dried for 10 h under high vacuum: **1′c** (44 mg, 35%). Yellowish solid. M.p. 112–114°. UV/VIS ($CHCl_3$): 342.0 (44300). ^{1}H-NMR ($CDCl_3$, 200 MHz): 9.06 (*s*, 1 H); 8.45 (*s*, 1 H); 8.29 (*d*, 2 H); 7.90–7.51 (*m*, 6 H); 6.90 (*t*, 2 H); 4.35 (*t*, 4 H); 1.70 (*t*, 4 H); 1.57–1.19 (*m*, 12 H); 0.89 (*t*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 161.8; 158.9; 156.9; 147.3; 137.4; 131.1; 116.9; 110.2; 109.7; 42.5; 31.6; 26.7; 24.6; 22.6; 14.0. FAB-MS: 487.2 (100, $[M+H]^+$). HR-FAB-MS: 487.3289 ($[C_{28}H_{38}N_8+H]^+$; calc. 487.3298). Anal. calc. for $C_{28}H_{38}N_8$: C 69.10, H 7.87, N 23.03; found: C 68.90, H 7.65, N 23.13.

Pyrimidine-4,6-dicarboxaldehyde Bis[(2-hydroxyethyl)(pyridin-2-yl)hydrazone] (**1′d**). As described for **1b**, with **26d** (113 mg, 0.738 mmol), **14a** (50 mg, 0.367 mmol), and EtOH (5 ml): **1′d** (62 mg, 41%). Yellow solid. M.p. 195–196°. UV/VIS ($CHCl_3$): 333.0 (37800). IR (KBr): 3427*m* (br.), 1591*m*, 1560*s*, 1546*s*, 1437*s*, 1389*w*, 1349*s*, 772*m*. ^{1}H-NMR ($CDCl_3/CD_3OD$ 1:1, 200 MHz): 9.08 (*d*, 1 H); 8.40 (*d*, 1 H); 8.27 (*d*, 2 H); 7.82–7.65 (*m*, 6 H); 6.98 (*t*, 2 H); 4.52 (*t*, 4 H); 4.35 (*s*, 2 H); 3.99 (*t*, 4 H). ^{13}C-NMR ($CDCl_3/CD_3OD$ 1:1, 50 MHz): 165.6; 162.2; 161.1; 150.9; 142.1; 134.8; 121.7; 114.8; 114.7; 61.96; 49.44. EI-MS: 406.3 (11, M^+), 1643 (100), 120.3 (17). FAB-MS: 407.1 (100, $[M+H]^+$). HR-FAB-MS: 407.1950 ($[C_{20}H_{22}N_8O_2+H]^+$; calc. 407.1944).

2-Phenylpyrimidine-4,6-dicarboxaldehyde Bis[methyl(pyridin-2-yl)hydrazone] (**1′e**). As described for **1b**, with **14b** (30 mg, 0.142 mmol), **26a** (40 mg, 0.325 mmol), and EtOH (4 ml): **1′e** (36 mg, 60%). Yellow solid. M.p. 259–261°. UV/VIS ($CHCl_3$): 339.0. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.57–8.45 (*m*, 2 H); 8.36 (*s*, 1 H); 8.29 (*d*, 2 H); 7.87 (*d*, 2 H); 7.77 (*s*, 2 H); 7.67 (*t*, 2 H); 7.58–7.45 (*m*, 3 H); 6.91 (*t*, 2 H); 3.78 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 164.8; 162.1; 157.1; 147.1; 137.9; 137.6; 132.9; 130.5; 128.5; 128.2; 116.9; 110.4; 107.7; 30.0. FAB-MS: 423.2 (100, $[M+H]^+$). HR-FAB-MS: 423.2048 ($[C_{24}H_{22}N_8+H]^+$; calc. 423.2046).

Pyrimidine-4,6-dicarboxaldehyde Bis[methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone] (**2a**). As described for **1b**, with **10a** (250 mg, 0.973 mmol), **14a** (66 mg, 0.485 mmol), and EtOH (10 ml) for 5 h: **2a** (235 mg, 39%). Yellow solid. M.p. 298–300° (dec.) (recryst. from $CHCl_3$/MeCN). UV/

VIS ($CHCl_3$): 316.0 (68100). IR (KBr): 1589*s*, 1480*s*, 1400*m*, 1351*m*, 1338*m*, 1270*m*, 1230*m*, 1188*s*, 1154*m*, 1075*s*, 1023*s*, 978*s*, 843*m*, 785*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 9.18 (*d*, 1 H); 8.74 (*d*, 1 H); 8.29 (*d*, 2 H); 8.19 (*d*, 2 H); 7.76 (*s*, 2 H); 7.72 (*d*, 2 H); 7.54 (*s*, 2 H); 7.53 (*d*, 2 H); 7.13 (*t*, 2 H); 6.91 (*t*, 2 H); 3.54 (*s*, 6 H); 3.35 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.1; 161.7; 161.6; 159.2; 156.3; 153.9; 149.1; 136.9; 135.4; 134.1; 122.2; 119.3; 109.4; 89.8; 29.9; 29.5. 2D-NMR (300 MHz): COSY, NOESY. FAB-MS: 615.2 (100, $[M+H]^+$). HR-FAB-MS: 615.2912 ($[C_{30}H_{30}N_{16}+H]^+$; calc. 615.2918). Anal. calc. for $C_{30}H_{30}N_{16}$: C 58.62, H 4.92, N 36.46; found: C 58.54, H 4.81, N 36.32.

2-Phenylpyrimidine-4,6-dicarboxaldehyde Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-pyrimidin-4-yl]hydrazone} (**2b**). As described for **1b**, with a suspension of **10a** (23 mg, 89.5 μmol), **14b** (9 mg, 42.5 μmol), and EtOH (0.5 ml) (concentration not necessary): **2b** (22 mg, 75%). Yellowish solid. M.p. 368–370° (dec.). UV/VIS ($CHCl_3$): 314.0 (78200). IR (KBr): 3037*w*, 1591*s*, 1482*s*, 1427*s*, 1398*m*, 1356*s*, 1275*s*, 1192*s*, 1154*m*, 1074*s*, 1024*s*, 896*m*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.67 (*s*, 1 H); 8.61–8.54 (*m*, 2 H); 8.32 (*d*, 2 H); 8.23 (*s*, 2 H); 7.91 (*s*, 2 H); 7.80 (*d*, 2 H); 7.65–7.51 (*m*, 7 H); 7.18 (*t*, 2 H); 6.94 (*t*, 2 H); 3.64 (*s*, 6 H); 3.57 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.2; 161.7; 159.8; 156.2; 154.0; 153.5; 149.1; 137.0; 135.4; 135.0; 131.5; 130.8; 128.7; 128.2; 122.2; 119.32; 107.2; 89.8; 29.9; 29.5. FAB-MS: 691.7 (100, $[M+H]^+$). HR-FAB-MS: 691.3226 ($[C_{36}H_{34}N_{16}+H]^+$; calc. 691.3231).

Pyridine-2-carboxaldehyde {(Pyrimidine-4,6-diyl)bis[ethylidyne(1-methylhydrazin-1-yl-2-ylidene)pyrimidine-6,4-diyl]}bis(methylhydrazone) (**2d**). As described for **1b**, with **10a** (50 mg, 0.195 mmol), **14c** (16 mg, 0.098 mmol), and EtOH (3 ml) for 15 h: **2d** (19 mg, 30%). Yellow solid. M.p. 238–239°. UV/VIS ($CHCl_3$): 330.0 (42600). IR (KBr): 1589*s*, 1484*m*, 1430*s*, 1397*m*, 1278*m*, 1189*m*, 1145*m*, 1077*m*, 1021*m*, 990*m*, 834*w*, 774*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 9.39 (*s*, 1 H); 9.29 (*s*, 1 H); 8.50 (*d*, 2 H); 8.31 (*s*, 2 H); 7.69 (*d*, 2 H); 7.41–7.36 (*m*, 4 H); 7.28 (*t*, 2 H); 7.07 (*t*, 2 H); 3.50 (*s*, 6 H); 3.12 (*s*, 6 H); 2.53 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 165.1; 164.6; 162.9; 160.2; 160.1; 159.4; 157.0; 155.5; 149.9; 136.9; 136.4; 123.2; 120.4; 110.2; 90.5; 37.6; 29.4; 16.3. 2D-NMR (300 MHz): COSY, NOESY. FAB-MS: 643.6 (100, $[M+H]^+$). HR-FAB-MS: 643.3226 ($[C_{32}H_{34}N_{16}+H]^+$; calc. 643.3231).

Pyrimidine-4,6-dicarboxaldehyde Bis{hexyl[6-[1-hexyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone} (**2e**). As described for **1b**, with **10c** (42 mg, 0.105 mmol), **14a** (7 mg, 0.052 mmol), and EtOH (3 ml) for 4 h. The mixture was cooled and the EtOH evaporated. Purification by prep. TLC (Al_2O_3, AcOEt/hexane 15:85) gave, after drying for 10 h under high vacuum, **2e** (19 mg, 40%). ^{1}H-NMR ($CDCl_3$, 200 MHz): 9.17 (*s*, 1 H); 8.68 (*s*, 1 H); 8.27 (*d*, 2 H); 8.19 (*s*, 2 H); 7.81–7.70 (*m*, 4 H); 7.55 (*s*, 2 H); 7.42 (*s*, 2 H); 7.14 (*t*, 2 H); 6.88 (*t*, 2 H); 4.21–4.08 (*m*, 8 H); 1.76–1.25 (*m*, 32 H); 1.00–0.78 (*m*, 12 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 162.0; 161.9; 161.4; 159.1; 156.6; 154.2; 149.0; 136.5; 136.1; 135.6; 133.3; 122.3; 119.3; 109.0; 89.5; 42.8; 42.3; 31.7; 25.2; 24.8; 22.8; 14.1. FAB-MS: 895.5 (100, $[M+H]^+$). HR-FAB-MS: 895.6056 ($[C_{50}H_{70}N_{16}+H]^+$; calc. 895.6048).

2-Phenylpyrimidine-4,6-dicarboxaldehyde Bis{hexyl[6-[1-hexyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone} (**2f**). As described for **1b**, with **14b** (20 mg, 94.3 μmol), **10c** (85 mg, 214.1 μmol), and EtOH (10 ml) for 5 h. The mixture was cooled, the EtOH evaporated, and the residue purified by FC (Al_2O_3, AcOEt/hexane 1:9): **2f** (54 mg, 60%). ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.62–8.50 (*m*, 3 H); 2.28 (*d*, 2 H); 8.20 (*s*, 2 H); 7.88 (*s*, 2 H); 7.79 (*d*, 2 H); 7.62–7.48 (*m*, 5 H); 7.46 (*s*, 2 H); 7.14 (*t*, 2 H); 6.88 (*t*, 2 H); 4.27–4.05 (*m*, 8 H); 1.85–1.12 (*m*, 32 H); 1.05–0.70 (*m*, 12 H). ^{13}C-NMR ($CDCl_3$, 40 MHz): 162.4; 162.1; 156.6; 154.2; 148.9; 136.5; 135.6; 134.3; 130.9; 128.9; 128.3; 119.3; 89.6; 65.6; 42.8; 42.4; 30.7; 30.1; 29.8; 26.7; 22.8; 14.1. 2D-NMR (200 MHz): NOESY. FAB-MS: 971.6 (100, $[M+H]^+$). HR-FAB-MS: 961.6336 ($[C_{56}H_{74}N_{16}+H]^+$; calc. 971.6361).

Pyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone} 6,6′-[(Pyrimidine-4,6-diyl)bis(methylhydrazone)] (**3a**). As described for **1b**, with **11a** (146 mg, 0.389 mmol), **9b** (30 mg, 0.179 mmol), and EtOH (6 ml) for 6 h: **3a** (120 mg, 76%). Yellowish solid. M.p. >350° (dec.). UV/VIS ($CHCl_3$): 306.0 (80500). IR (KBr): 3023*w*, 1591*s*, 1477*s*, 1429*m*, 1399*m*, 1339*w*, 1270*w*, 1023*s*, 906*m*, 784*m*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.86 (*s*, 2 H); 8.36 (*s*, 2 H); 8.33 (*s*, 2 H); 8.18 (*d*, 2 H); 7.90 (*s*, 1 H); 7.54–7.40 (*m*, 10 H); 7.20 (*s*, 1 H); 6.97 (*t*, 2 H); 6.78 (*t*, 2 H); 3.57 (*s*, 6 H); 3.54 (*s*, 6 H); 3.43 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 161.7; 161.1; 160.7; 159.1; 156.6; 155.7; 153.6; 148.9; 136.9; 135.2; 134.2; 134.1; 122.2; 119.2; 90.8; 89.4; 30.0; 29.8; 29.5. 2D-NMR (500 MHz): COSY, ROESY. FAB-MS: 883.2 (100, $[M+H]^+$). HR-FAB-MS: 883.4107 ($[C_{42}H_{42}N_{24}+H]^+$; calc. 883.4103). Anal. calc. for $C_{42}H_{42}N_{24}\cdot CH_2Cl_2$: C 53.36, H 4.58, N 34.75; found: C 53.70, H 4.63, N 35.02.

2-Phenylpyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone} 6,6′-[(Pyrimidine-4,6-diyl)bis(methylhydrazone)] (**3b**). As described for **1b**, with a suspension of **11b** (14 mg, 31.0 μmol), **9b** (2 mg, 11.9 μmol), and EtOH (2 ml) for 15 h: **3b** (8 mg, 65%).

Yellow solid. M.p. >350°. UV/VIS ($CHCl_3$): 307.0 (66700). IR (KBr): 2922*m*, 1590*s*, 1482*s*, 1371*m*, 1025*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 8.48 (*d*, 4 H); 8.31 (*s*, 2 H); 8.18 (*d*, 2 H); 7.92 (*s*, 1 H); 7.89 (*s*, 2 H); 7.61–7.54 (*m*, 12 H); 7.47 (*d*, 2 H); 7.46 (*s*, 2 H); 7.24 (*s*, 1 H); 6.96 (*t*, 2 H); 6.78 (*t*, 2 H); 3.59 (*s*, 6 H); 3.52 (*s*, 6 H); 3.49 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 168.9; 164.6; 161.9; 161.6; 161.2; 161.0; 156.0; 155.8; 137.6; 135.3; 135.1; 132.0; 130.6; 128.5; 128.3; 126.2; 122.2; 119.4; 106.8; 89.1; 30.0; 29.9; 29.7. 2D-NMR (500 MHz): COSY, ROESY. FAB-MS: 1035.8 (100, $[M+H]^+$). HR-FAB-MS: 1035.4734 ($[C_{54}H_{50}N_{24}+H]^+$; calc. 1035.4729).

2-Phenylpyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-2-phenylpyrimidin-4-yl}hydrazone} 6,6′-[(2-Phenylpyrimidine-4,6-diyl)bis(methylhydrazone)] (**3c**). A soln. of **11b** (20 mg, 0.035 mmol) and **9c** (4.6 mg, 0.018 mmol) in $CHCl_3$ (3 ml) was stirred at 45° for 2 h under Ar. The mixture was evaporated and the residue submitted to FC (Al_2O_3, $CHCl_3$): **3b** (15 mg, 66%). M.p. >250°. UV/VIS ($CHCl_3$): 305.0 nm (44800). IR (KBr): 1591*s*, 1550*s*, 1482*m*, 1390*s*, 1370*m*, 1248*w*, 1169*m*, 1083*w*, 1030*m*, 980*w*, 904*w*, 753*w*, 695*m*. ^{1}H-NMR (CD_2Cl_2, 500 MHz): 8.44 (*s*, 2 H); 8.25 (*m*, 2 H); 8.20 (*d*, 4 H); 8.02 (*d*, 4 H); 7.92 (*d*, 2 H); 7.62 (*m*, 4 H); 7.55 (*m*, 7 H); 7.47 (*s*, 2 H); 7.34 (*m*, 5 H); 7.23 (*m*, 8 H); 6.99 (*t*, 2 H); 6.71 (*t*, 2 H); 3.72 (*s*, 6 H); 3.66 (*s*, 6 H); 3.60 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 164.3; 162.0; 161.4; 161.2; 161.0; 135.1; 130.0; 129.9; 129.8; 129.7; 129.6; 128.0; 127.9; 127.8; 127.7; 121.8; 106.7; 87.3; 31.7; 29.7. FAB-MS: 1263.5 (100, $[M+H]^+$).

2-Phenylpyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-2-phenylpyrimidin-4-yl]hydrazone} 6,6′-{[2-(4-Methylphenyl)pyrimidine-4,6-diyl]bis(methylhy drazone)} (**3d**). As described for **1b**, with **11a** (6 mg, 15.9 μmol), **9d** (2 mg, 7.8 μmol), and EtOH (2 ml) for 8 h: **3d** (4 mg, 53%). Yellowish solid. M.p. >350° (dec.). UV/VIS ($CHCl_3$): 305.0 (62000). ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.88 (*d*, 2 H); 8.39 (*s*, 2 H); 8.37 (*d*, 2 H); 8.17 (*d*, 2 H); 7.92 (*d*, 2 H); 7.57 (*d*, 2 H); 7.51 (*s*, 2 H); 7.49 (*s*, 4 H); 7.42 (*s*, 2 H); 7.33 (*d*, 2 H); 7.09 (*s*, 1 H); 6.94 (*t*, 2 H); 6.63 (*t*, 2 H); 3.63 (*s*, 6 H); 3.61 (*s*, 6 H); 3.59 (*s*, 6 H); 2.51 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.7; 162.2; 161.6; 161.4; 160.9; 159.0; 156.5; 153.5; 148.9; 148.5; 148.2; 141.1; 137.3; 135.3; 134.5; 133.6; 129.0; 128.0; 122.2; 119.1; 119.0; 108.9; 90.2; 88.5; 30.1; 29.9; 29.7. 2D-NMR (300 MHz): ^{1}H,^{13}C HMQC, ^{1}H,^{13}C HMBC. FAB-MS: 973.5 (100, $[M+H]^+$). HR-FAB-MS: 973.4567 ($[C_{49}H_{48}N_{24}+H]^+$; calc. 973.4572).

2-Phenylpyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-2-phenylpyrimidin-4-yl}hydrazone} 6,6′-{[2-(3,4,5-Trimethoxyphenyl)pyrimidine-4,6-diyl]bis(methylhydrazone)} (**3e**). As described for **3c**, with **11c** (10 mg, 0.019 mmol), 4,6-bis(1-methylhydrazino)-2-(3,4,5-trimethoxyphenyl)pyrimidine (**9e**; 3 mg, 0.009 mmol), and $CHCl_3$ (3 ml): **2** (22 mg, 85%). M.p. >250°. ^{1}H-NMR (CD_2Cl_2, 500 MHz): 8.32 (*s*, 2 H); 8.18 (*m*, 2 H); 8.08 (*m*, 4 H); 8.02 (*d*, 2 H); 7.68 (*d*, 2 H); 7.64 (*s*, 2 H); 7.59 (*s*, 2 H); 7.55 (*s*, 4 H); 7.41 (*s*, 2 H); 7.23 (*m*, 12 H); 7.10 (*s*, 1 H); 6.96 (*t*, 2 H); 6.58 (*t*, 2 H); 4.08 (*s*, 6 H); 3.99 (*s*, 3 H); 3.77 (*s*, 6 H); 3.66 (*s*, 6 H); 3.61 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 164.5; 162.5; 162.2; 161.8; 161.4; 161.0; 153.8; 153.0; 148.3; 137.64; 137.2; 135.6; 135.4; 130.2; 129.9; 128.2; 128.0; 127.9; 127.8; 121.9; 119.3; 106.8; 105.3; 88.9; 87.5; 60.9; 56.3; 30.2; 30.2; 29.8; 29.6. FAB-MS: 1353.7 (100, $[M+H]^+$).

Pyrimidine-4,6-dicarboxaldehyde Bis{methyl[6-[1-methyl-2-{[6-{[2-methyl-2-[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl}hydrazono}methyl]pyrimidin-4-yl]methylene}hydrazino}pyrimidin-4-yl]-hydrazone} (**4**). As described for **1b**, with a suspension of **12a** (47 mg, 89.4 μmol), **14a** (6 mg, 44.1 μmol), and EtOH (4 ml) for 12 h: **4** (15 mg, 30%). Yellowish solid. M.p. >300° (dec.). UV/VIS ($CHCl_3$): 302. IR (KBr): 2928*w*, 1590*s*, 1481*s*, 798*m*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.74 (*s*, 2 H); 8.51 (*s*, 1 H); 8.23 (*s*, 2 H); 8.13 (*d*, 2 H); 8.12 (*s*, 2 H); 8.05 (*s*, 2 H); 7.98 (*s*, 1 H); 7.44–7.29 (*m*, 8 H); 7.20 (*s*, 2 H); 7.12 (*s*, 2 H); 7.05 (*s*, 2 H); 6.86 (*t*, 2 H); 6.73 (*t*, 2 H); 3.46–3.40 (*m*, 24 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 164.3; 161.0; 160.3; 159.7; 158.9; 156.4; 156.1; 153.9; 148.9; 141.8; 139.0; 136.7; 135.2; 134.2; 134.0; 133.9; 128.5; 122.0; 119.0; 117.5; 108.8; 90.2; 89.1; 87.5; 29.9; 29.8; 29.7; 29.5. 2D-NMR (500 MHz): COSY, ROESY. FAB-MS: 1151.4 (100, $[M+H]^+$). HR-FAB-MS: 1151.5285 ($[C_{54}H_{54}N_{32}+H]^+$; calc. 1151.5287).

Pyrimidine-4,6-dicarboxaldehyde 4,4′-Bis{methyl[6-[1-methyl-2-{[6-{[2-methyl-2-[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazono}methyl]pyrimidin-4-yl}methylene}hydrazino}pyrimidin-4-yl]hydrazone} 6,6′-[(Pyrimidine-4,6-diyl)bis(methylhydrazone)] (**5**). A soln. of **13** (63 mg, 0.098 mmol; purified by FC (Al_2O_3, $CHCl_3$/EtOH 98:2) and **9a** (8 mg, 0.048 mmol) in EtOH/$CHCl_3$ 3:1 (5 ml) was heated to reflux for 48 h. Then, the mixture was cooled, concentrated under vacuum (to remove the $CHCl_3$), and filtered. The precipitate was washed with EtOH and dried for 10 h under high vacuum: **5** (40 mg, 59%). Yellowish solid. M.p. >350° (dec.). UV/VIS ($CHCl_3$): 300.0 (165000). IR (KBr): 2925*w*, 1597*s*, 1479*s*, 1397*m*, 1022*m*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.73 (*s*, 2 H); 8.43 (*s*, 2 H); 8.24 (*s*, 1 H); 8.22 (*s*, 2 H); 8.13 (*d*, 2 H); 8.06 (*s*, 2 H); 7.98 (*s*, 2 H); 7.78 (*s*, 2 H); 7.37–7.27 (*m*, 10 H); 7.13 (*s*, 2 H); 7.06 (*s*, 2 H); 6.97 (*s*, 2 H); 6.93 (*s*, 1 H); 6.89 (*s*, 2 H); 6.83 (*t*, 2 H); 6.72 (*t*, 2 H); 3.45–3.40 (*m*, 24 H); 3.29 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 161.9; 161.3; 161.0; 160.8; 160.7; 160.5; 160.4; 159.6; 159.3; 158.9; 158.8; 156.3; 156.0; 153.4; 148.9; 135.2; 134.2; 134.0; 133.9; 133.7;

122.1; 118.9; 108.7; 108.6; 90.0; 89.4; 89.1; 76.6; 30.9; 30.0; 29.9; 29.8; 29.5. 2D-NMR (300 MHz): COSY, NOESY, ^{1}H,^{13}C HMQC. FAB-MS: 1419.6 (100, $[M+H]^+$).

Pyrimidine-4,6-dicarboxaldehyde Methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone Methyl(pyridin-2-yl)hydrazone (**6**). *a*) As described for **1b**, with **11a** (4 mg, 10.7 μmol), **26a** (2 mg, 16.3 μmol), and EtOH (3 ml) for 4 h: **6** (5 mg, 98%).

b) As described for **1b**, with **10a** (5 mg, 19.5 μmol), **15** (5 mg, 20.7 μmol), and EtOH (3 ml): **6** (9 mg, 96%). Yellowish solid. M.p. 262–264°. UV/VIS ($CHCl_3$): 336.0 (52600). IR (KBr): 3025*w*, 1592*s*, 1478*s*, 1398*m*, 1352*m*, 1235*w*, 1129*m*, 1074*m*, 1023*m*, 977*m*, 906*m*, 777*s*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 9.17 (*s*, 1 H); 8.59 (*s*, 1 H); 8.54 (*s*, 1 H); 8.25 (*d*, 1 H); 8.04 (*d*, 1 H); 8.01 (*s*, 1 H); 7.86 (*d*, 1 H); 7.79 (*s*, 1 H); 7.70 (*s*, 1 H); 7.66 (*s*, 1 H); 7.40 (*d*, 1 H); 7.24–7.20 (*m*, 2 H); 6.93 (*t*, 1 H); 6.70 (*t*, 1 H); 3.76 (*s*, 3 H); 3.72 (*s*, 3 H); 3.64 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.6; 162.1; 161.4; 159.0; 156.8; 156.0; 154.1; 148.9; 146.5; 137.8; 136.9; 135.7; 134.7; 131.4; 122.5; 119.4; 117.0; 110.4; 109.8; 89.4; 85.7; 30.1; 29.9; 29.6. 2D-NMR (500 MHz): COSY, NOESY. EI-MS: 480.3 (100, M^+), 402.3 (20, $[M-78]^+$), 268.2 (54, $[M-132]^+$), 134.3 (100, $[M-264]^+$). FAB-MS: 481.3 (100, $[M+H]^+$). HR-FAB-MS: 481.2341 ($[C_{24}H_{24}N_{12}+H]^+$; calc. 481.2325).

Pyrimidine-4,6-dicarboxaldehyde 4,4′-Bis[methyl(pyridin-2-yl)hydrazone] 6,6′-[(Pyrimidine-4,6-diyl)bis-(methylhydrazone)] (**7**). As described for **1b**, with **15** (8 mg, 33.2 μmol), **9b** (2 mg, 11.9 μmol), and EtOH (1 ml) for 8 h: **7** (7.5 mg, 73%). Yellowish solid. M.p. >250°. UV/VIS ($CHCl_3$): 331.0 (67000). IR (KBr): 1595*s*, 1564*s*, 1476*s*, 1393*m*, 1346*m*, 1232*m*, 1155*w*, 1127*m*, 1024*m*, 979*s*, 768*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.61 (*s*, 2 H); 8.57 (*s*, 1 H); 8.31 (*s*, 2 H); 8.16 (*s*, 1 H); 8.14 (*d*, 2 H); 7.51 (*s*, 2 H); 7.34 (*s*, 2 H); 7.22 (*d*, 2 H); 7.17 (*t*, 2 H); 6.77 (*t*, 2 H); 3.74 (*s*, 6 H); 3.56 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 162.9; 161.1; 160.5; 158.7; 157.1; 155.8; 146.8; 136.7; 135.1; 131.1; 117.0; 109.9; 109.5; 89.8; 29.9; 29.8. 2D-NMR (300 MHz): COSY, NOESY. FAB-MS: 615.2 (100, $[M+H]^+$). HR-FAB-MS: 615.2944 ($[C_{30}H_{30}N_{16}+H]^+$; calc. 615.2918).

4,6-Dichloro-2-(3,4,5-trimethoxyphenyl)pyrimidine (**8d**). $POCl_3$ (20 ml) was slowly added to **19** (0.28 g, 1.007 mmol), and the suspension was heated to reflux for 5 h. The excess $POCl_3$ was evaporated, the remaining paste dissolved in CH_2Cl_2, and the soln. washed consecutively with ice water and sat. $NaHCO_3$ soln. dried ($MgSO_4$), and evaporated: The crude product was submitted to FC (SiO_2, CH_2Cl_2/AcOEt 15:5) and recrystallized from MeOH: **8d** (0.65 g, 82%). M.p. 168°. IR (KBr): 3478*w*, 1655*s*, 1523*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.70 (*s*, 2 H); 7.23 (*s*, 1 H); 3.17 (*s*, 6 H); 3.12 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 165.32; 161.1; 153.4; 141.8; 118.4; 61.0; 56.4; 26.0. EI-MS: 314.1. Anal. calc. for $C_{13}H_{12}Cl_2N_2O_3$: C 41.54, H 3.84, N 8.81; found: C 41.40, H 3.65, N 8.01.

4,6-Dihydrazino-2-(3,4,5-trimethoxyphenyl)pyrimidine (**9a**). To a soln. of **8d** (700 mg, 2.21 mmol) in EtOH (30 ml) was added hydrazine monohydrate (2.2 ml, 4.5 mmol). The mixture was heated to reflux for 72 h under Ar. The soln. was allowed to cool to r.t. and then cooled further to 0°. The crystalline solid that formed was filtered, washed with EtOH, and air-dried: **5** (470 mg, 61%). M.p. 223°. IR (KBr): 1651*s*, 1575*s*, 1542. ^{1}H-NMR ((D$_6$)DMSO, 200 MHz): 8.84 (*s*, 1 H); 7.58 (*s*, 2 H); 6.68 (*s*, 1 H); 4.53 (*s*, 2 H); 3.85 (*s*, 6 H); 3.73 (*s*, 3 H). EI-MS: 306.3. Anal. calc. for $C_{13}H_{18}N_6O_3 \cdot 0.25$ HCl: C 41.81, H 5.81, N 26.60; found: C 41.15, H 5.54, N 26.20.

4,6-Bis(1-methylhydrazino)pyrimidine (**9b**). Under magnetic stirring, 4,6-dichloropyrimidine (**8a**; 1 g, 6.711 mmol) was slowly added by portions to ice-cooled methylhydrazine (15 g, 326.087 mmol). The mixture was refluxed for 2 h under Ar. After cooling, methylhydrazine was evaporated, K_2CO_3 (1 g, 7.246 mmol) and $CHCl_3$ (150 ml) were added to the solid residue, and the mixture was stirred during 10 min. The liquid phase was filtered. The solid-liquid extraction procedure was repeated 3 times with $CHCl_3$ (without adding K_2CO_3), and the combined liquid fraction was evaporated: **9b** (quant.), NMR pure and so used without further purification. White solid, unstable in air. M.p. 143–145°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.17 (*s*, 1 H); 6.18 (*s*, 1 H); 3.98 (*s*, 4 H); 3.23 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 164.7; 156.9; 80.9; 39.9. FAB-MS: 169.0 (100, $[M+H]^+$). HR-FAB-MS: 169.1202 ($[C_6H_{12}N_6+H]^+$; calc. 169.1202).

4,6-Bis(1-methylhydrazino)-2-phenylpyrimidine (**9c**). As described for **9a**, with 4,6-dichloro-2-phenylpyrimidine (**8b**; 2.5 g, 11.2 mmol), EtOH (30 ml), and methylhydrazine (2.4 ml, 45.1 mmol) for 48 h: **9c** (300 mg, 70%). M.p. 126°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.40 (*m*, 2 H); 7.42 (*m*, 3 H); 6.14 (*s*, 1 H); 3.37 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 172.1; 165.4; 161.9; 139.0; 129.9; 128.1; 79.3; 39.9. FAB-MS: 245.1 (100, $[M+H]^+$). Anal. calc. for $C_{12}H_{16}N_6$: C 59.00, H 6.60, N 34.40; found: C 58.76, H 6.76, N 34.20.

4,6-Bis(1-methylhydrazino)-2-(4-methylphenyl)pyrimidine (**9d**). As described for **9b**, with 4,6-dichloro-2-(4-methylphenyl)pyrimidine (**8c**; 0.3 g, 1.255 mmol), methylhydrazine (**25a**; 3 g, 65.217 mmol), K_2CO_3 (0.3 g, 2.174 mmol), and $CHCl_3$ (100 ml) (1 solid-liquid extraction): **9d** (quant.). White solid. M.p. 177–179°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.29 (*d*, 2 H); 7.22 (*d*, 2 H); 6.09 (*s*, 1 H); 4.20 (*s*, 4 H); 3.35 (*s*, 6 H); 2.39 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 163.4; 162.2; 139.9; 136.2; 128.8; 127.9; 79.1; 40.0; 21.5. FAB-MS: 259.4 (100, $[M+H]^+$).

4,6-Bis(1-methylhydrazino)-2-(3,4,5-trimethoxyphenyl)pyrimidine (**9e**). As described for **9a**, with **8d** (400 mg, 1.27 mmol), EtOH (30 ml), and methylhydrazine (0.350 ml, 6.34 mmol) for 48 h. The crude solid was redissolved in $CHCl_3$, the soln. washed with sat. aq. NH_4Cl soln. dried ($MgSO_4$), and the solvent removed by distillation on a waterbath: **9e** (300 mg, 70%) after air-drying. M.p. 170°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.68 (*s*, 2 H); 6.2 (*s*, 1 H); 4.12 (*s*, 2 H); 3.88 (*s*, 3 H); 3.53 (*s*, 6 H); 3.14 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 165.5; 161.8; 152.1; 134.5; 71.2; 60.1; 56.2; 40.1; 25.4; 13.1. FAB-MS: 335.6 (100, $[M+H]^+$). Anal. calc. for $C_{15}H_{22}N_6O_3$: C 53.88, H 6.63, N 25.13; found: C 54.01, H 6.62, N 24.00.

4,6-Bis(1-hexylhydrazino)pyrimidine (**9f**). As described for **9b**, with **8a** (1 g, 6.711 mmol), hexylhydrazine (**25b**; 20 g, 172.414 mmol) (at 150° for 3 h), K_2CO_3 (1 g, 7.246 mmol), and CH_2Cl_2 (50 ml). The solid/liquid mixture was stirred for 20 min and then filtered, and the filtrate evaporated. The residue was dissolved in the minimal volume of CH_2Cl_2, and heptane was added until a light cloudiness appeared. The mixture was put in a fridge (4°) overnight, and the resulting precipitate filtered: **9f** (0.85 g, 41%). White solid, unstable in air and stored under Ar in a freezer. M.p. 58–60°. IR (KBr): 3322*w*, 3188*w*, 2927*s*, 2855*s*, 1587*s*, 1474*s*, 1372*w*, 1332*w*, 1252*w*, 1189*w*, 972*m*, 895*m*, 807*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.18 (*s*, 1 H); 6.19 (*s*, 1 H); 3.87 (*s*, 4 H); 3.62 (*t*, 4 H); 1.62 (*t*, 4 H); 1.43–1.23 (*m*, 12 H); 0.86 (*t*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 164.3; 157.0; 80.4; 51.2; 31.7; 26.5; 22.6; 13.9. EI-MS: 308.2 (42, M^+), 292.2 (100), 223.2 (38), 222.1 (62). FAB-MS: 309.2 (100, $[M+H]^+$). HR-FAB-MS: 309.2771 ($[C_{16}H_{32}N_6+H]^+$; calc. 309.2767).

4,6-Bis[1-(prop-2-enyl)hydrazino]pyrimidine (**9g**). As described for **9b**, with **8a** (0.1 g, 0.671 mmol), (prop-2-enyl)hydrazine (**25d**; 2 g, 27.778 mmol) (for 3 h), K_2CO_3 (0.1 g, 0.724 mmol), and $CHCl_3$ (100 ml) (1 solid-liquid extraction): **9g** (quant.). ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.10 (*s*, 1 H); 6.44 (*s*, 1 H); 6.85–5.60 (*m*, 2 H); 5.05–5.25 (*m*, 4 H); 4.24 (*dd*, 4 H); 3.76 (*s*, 4 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 164.9; 157.1; 132.7; 117.9; 82.0; 54.1. EI-MS: 220.1 (35, M^+), 179 (100, $[M-41]^+$), 138 (97, $[M-82]^+$). FAB-MS: 221.1 (100, $[M+H]^+$). HR-FAB-MS: 221.1505 ($[C_{10}H_{16}N_6+H]^+$; calc. 221.1515).

Pyridine-2-carboxaldehyde Methyl[6-(1-methylhydrazino)pyrimidin-4-yl]hydrazone (**10a**). A soln. of pyridine-2-carboxaldehyde (1.14 g, 10.654 mmol) and **9b** (2.5 g, 14.881 mmol) in EtOH (500 ml) was stirred at r.t. under Ar for 3 h. Then, the soln. was filtered, the EtOH from the filtrate evaporated, and the solid residue purified by FC (Al_2O_3, $CHCl_3$, then $CHCl_3$/EtOH 95:5: **10a** (2.1 g, 55%). White solid. M.p. 157–159°. UV/VIS ($CHCl_3$): 336.0. IR (KBr): 3294*w*, 3180*w*, 3000*w*, 2924*w*, 2853*w*, 1589*s*, 1490*s*, 1407*m*, 1284*s*, 1186*m*, 1109*m*, 1080*m*, 978*s*, 844*m*, 805*m*, 625*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.58 (*d*, 1 H); 8.32 (*s*, 1 H); 8.03 (*d*, 1 H); 7.81 (*s*, 1 H); 7.71 (*t*, 1 H); 7.21 (*t*, 1 H); 7.01 (*s*, 1 H); 4.11 (*s*, 2 H); 3.64 (*s*, 3 H); 3.34 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 164.5; 161.8; 156.4; 154.5; 148.9; 136.5; 136.2; 123.5; 119.2; 84.3; 39.6; 29.4. EI-MS: 257.2 (22, M^+), 179.2 (100). FAB-MS: 258.1 (100, $[M+H]^+$). HR-FAB-MS: 258.1471 ($[C_{12}H_{15}N_7+H]^+$; calc. 258.1467).

Pyridine-2-carboxaldehyde Methyl[6-(1-methylhydrazino)-2-phenylpyrimidin-4-yl]hydrazone (**10b**). As described for **10a**, with pyridine-2-carboxaldehyde (33 µl, 0.21 mmol), **9c** (170 mg, 0.61 mmol), and abs. EtOH (35 ml) for 4 h. FC (Al_2O_3, $CHCl_3$) gave **10b** (77 mg, 80%). White solid. M.p. 128°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.51 (*d*, 1 H); 8.44 (*m*, 2 H); 8.02 (*d*, 1 H); 7.85 (*s*, 1 H); 7.73 (*t*, 1 H); 7.45 (*m*, 3 H); 7.21 (*t*, 1 H); 6.16 (*s*, 1 H); 3.80 (*s*, 3 H); 3.44 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 214.6; 144.0; 130.7; 125.0; 122.1; 122.8; 117.5; 114.1; 24.3. HR-FAB-MS: 334.1777 ($[C_{18}H_{19}N_7+H]^+$; calc. 334.1780). Anal. calc. for $C_{18}H_{19}N_7$: C 64.85, H 5.74, N 29.41; found: C 65.2, H 6.01, N 27.10.

Pyridine-2-carboxaldehyde Hexyl[6-(1-hexylhydrazino)pyrimidin-4-yl]hydrazone (**10c**). As described for **10a**, with pyridine-2-carboxaldehyde (0.364 g, 3.402 mmol), **9f** (1.5 g, 4.870 mmol), and EtOH (300 ml). FC (Al_2O_3, $CHCl_3$/hexane 8:2 gave **10c** (0.9 g, 47%). ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.55 (*d*, 1 H); 8.29 (*s*, 1 H); 7.95 (*d*, 1 H); 7.79 (*s*, 1 H); 7.66 (*t*, 1 H); 7.17 (*t*, 1 H); 6.93 (*s*, 1 H); 4.22 (*t*, 2 H); 3.99 (*s*, 2 H); 3.66 (*t*, 2 H); 1.75–1.51 (*m*, 16 H); 0.91–0.75 (*m*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 172.4; 164.5; 162.2; 157.1; 155.1; 149.2; 136.3; 136.0; 122.8; 119.4; 84.3; 51.4; 42.1; 31.7; 26.5; 25.1; 22.7; 14.0. EI-MS: 397.2 (16, M^+), 319.3 (100), 292.3 (21). FAB-MS: 398.2 (100, $[M+H]^+$). HR-FAB-MS: 398.3044 ($[C_{22}H_{35}N_7+H]^+$; calc. 398.3032).

Pyrimidine-4,6-dicarboxaldehyde Mono{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl]hydrazone} (**11a**). A soln. of **10a** (450 mg, 1.751 mmol) and **14a** (500 mg, 3.676 mmol) in EtOH (150 ml) was stirred overnight at 40° under Ar. Then, the soln. was filtered and the precipitate washed with EtOH to give **2a** (150 mg, 28%), which was recrystallized from $CHCl_3$/EtOH. The filtrate was concentrated (1–2 ml) *in vacuo*, and MeCN (20–30 ml) was added. Then, the mixture was stirred at r.t. for 6 h to precipitate **11a**, which was filtered, washed with MeCN, and then dried under vacuum for 10 h: 330 mg (50%) of **11a**. Yellow solid. M.p. > 250° (dec.). UV/VIS ($CHCl_3$): 322.0 (50000). IR (KBr): 2922*w*, 1718*s*, 1595*s*, 1456*s*, 1332*s*, 1275*m*, 1239*m*, 1186*m*, 1155*m*, 1075*s*, 1025*s*, 980*s*, 837*s*, 783*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 1012 (*s*, 1 H); 9.39 (*s*, 1 H); 8.62 (*d*, 1 H); 8.51 (*s*, 1 H); 8.48 (*s*, 1 H); 8.28 (*d*, 1 H); 8.12 (*t*, 1 H); 7.95 (*s*, 1 H); 7.85 (*s*, 1 H); 7.80 (*s*, 1 H); 7.32 (*t*, 1 H); 3.73 (*s*, 3 H); 3.71 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 192.8; 163.8; 162.9; 162.1; 159.8; 157.4; 156.7;

154.1; 149.1; 139.1; 137.7; 133.9; 123.5; 119.8; 111.4; 77.7; 30.5; 29.9. EI-MS: 375.2 (37, M^+), 297.1 (100), 268.2 (73), 163.1 (58). FAB-MS: 376.4 (100, $[M+H]^+$). HR-FAB-MS: 376.1636 ($[C_{18}H_{17}N_9O+H]^+$; calc. 376.1634).

2-Phenylpyrimidine-4,6-dicarboxaldehyde Mono{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl}hydrazone} (**11b**). A soln. of **10a** (300 mg, 1.167 mmol) and **14b** (500 mg, 2.358 mmol) in EtOH (100 ml) was stirred at r.t. under Ar for 30 h. Then, the soln. was filtered, the filtrate concentrated (2–3 ml) *in vacuo*, MeCN (20–30 ml) added, and the precipitate filtered, washed with MeCN, and dried under vacuum for 10 h: **11b** (220 mg, 42%). Yellow solid. M.p. >250°. IR (KBr): 2928*w*, 1718*s*, 1591*s*, 1465*s*, 1393*s*, 1359*s*, 1277*m*, 1208*m*, 1155*m*, 1073*s*, 1023*s*, 980*s*, 690*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 10.24 (*s*, 1 H); 8.67–8.56 (*m*, 4 H); 8.39 (*s*, 1 H); 8.29 (*d*, 1 H); 8.16 (*t*, 1 H); 7.98 (*s*, 1 H); 7.91 (*s*, 1 H); 7.87 (*s*, 1 H); 7.62–7.49 (*m*, 3 H); 7.32 (*t*, 1 H); 3.81 (*s*, 3 H); 3.77 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 193.6; 167.7; 162.2; 158.4; 156.8; 154.3; 151.4; 143.5; 139.2; 137.8; 136.8; 135.0; 131.5; 128.9; 128.5; 123.6; 119.9; 109.8; 109.0; 88.8; 30.0; 29.8. EI-MS: 451.2 (29, M^+), 373.1 (100), 268.1 (81), 136.1 (49). FAB-MS: 452.2 (100, $[M+H]^+$). HR-FAB-MS: 452.1953 ($[C_{24}H_{21}N_9O+H]^+$; calc. 452.1947).

2-Phenylpyrimidine-4,6-dicarboxaldehyde Mono{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-2-phenylpyrimidin-4-yl}hydrazone} (**11c**) *and 2-Phenylpyrimidine-4,6-dicarboxaldehyde Bis{methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]-2-phenylpyrimidin-4-yl}hydrazone}* (**2c**). A soln. of **10b** (88 mg, 0.26 mmol) and **14b** (56 mg, 0.27 mmol) in $CHCl_3$ (20 ml) was stirred at r.t. for 2 h under Ar. The mixture was then evaporated and the residue purified by FC (Al_2O_3, $CHCl_3$): **11c** (70 mg, 60%) and **2c** (20 mg, 8%).

Data of **11c**: M.p. >250°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 10.23 (*s*, 1 H); 8.62 (*m*, 1 H); 8.58 (*m*, 2 H); 8.50 (*m*, 2 H); 8.44 (*s*, 1 H); 8.33 (*d*, 1 H); 8.18 (*t*, 1 H); 7.83 (*s*, 1 H); 7.53 (*m*, 6 H); 7.31 (*t*, 1 H); 7.11 (*d*, 2 H); 3.92 (*s*, 3 H); 3.87 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 193.6; 165.7; 164.2; 163.3; 162.6; 162.1; 158.1; 154.3; 149.0; 138.5; 137.9; 137.8; 136.7; 134.5; 131.4; 130.5; 128.7; 128.3; 128.1; 123.4; 119.9; 118.4; 115.2; 113.8; 108.8; 86.9; 30.4; 30.0; 29.7. FAB-MS: 529.4 (100, $[M+H]^+$). Anal. calc. for $C_{30}H_{25}N_9O \cdot 0.7\ C_2H_6O$: C 67.37, H 5.26, N 22.52; found: C 67.67, H 5.10, N 22.17.

Data of **2c**: M.p. >250°. UV/VIS ($CHCl_3$): 303.0 (83000). IR (KBr): 2921*m*, 1591*s*, 1551*s*, 1483*s*, 1429*m*, 1385*s*, 1368*s*, 1246*w*, 1168*m*, 1084*w*, 1029*s*, 981*w*, 901*w*, 802*w*, 752*w*, 698. ^{1}H-NMR ($CDCl_3$, 500 MHz): 8.64 (*s*, 1 H); 8.56 (*m*, 2 H); 8.40 (*m*, 4 H); 7.83 (*d*, 2 H); 7.63 (*s*, 2 H); 7.56 (*m*, 3 H); 7.50 (*m*, 6 H); 7.47 (*s*, 2 H); 7.13 (*t*, 2 H); 7.11 (*d*, 2 H); 7.15 (*s*, 2 H); 6.72 (*t*, 2 H); 3.84 (*s*, 6 H); 3.61 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 162.6; 162.2; 161.8; 165.1; 138.0; 137.7; 135.3; 130.8; 130.3; 128.7; 128.3; 128.2; 128.1; 122.9; 122.2; 119.3; 107.1; 87.9; 87.1; 30.2; 29.7. FAB-MS: 843.3 (100, $[M+H]^+$).

Pyrimidine-4,6-dicarboxaldehyde Methyl[6-(1-methylhydrazino)pyrimidin-4-yl]hydrazone Methyl{6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl}hydrazone (**12a**). A soln. of **11a** (410 mg, 1.093 mmol) and **9b** (350 mg, 2.083 mmol) in EtOH/$CHCl_3$ 7:3 (70 ml) was stirred at 35° under Ar for 15 h. Then, the soln. was filtered, the filtrate concentrated (3–4 ml) *in vacuo*, MeCN (20–30 ml) added, and the precipitate filtered, washed with MeCN, and dried under vacuum for 10 h: **12a** (360 mg, 63%). Yellow solid. M.p. >250°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 9.15 (*s*, 1 H); 8.63 (*s*, 1 H); 8.51 (*s*, 1 H); 8.31 (*d*, 1 H); 8.07 (*s*, 1 H); 7.95 (*s*, 1 H); 7.82–7.69 (*m*, 4 H); 7.15 (*t*, 1 H); 6.95 (*t*, 1 H); 6.69 (*s*, 1 H); 3.75 (*s*, 3 H); 3.73 (*s*, 3 H); 3.58 (*s*, 3 H); 3.07 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 165.1; 164.2; 162.9; 162.8; 161.7; 161.5; 159.2; 157.1; 156.5; 153.7; 149.3; 138.5; 135.7; 134.9; 133.5; 122.7; 119.5; 109.9; 88.8; 85.4; 39.7; 30.23; 29.9; 29.8. FAB-MS: 526.4 (100, $[M+H]^+$). HR-FAB-MS: 526.2667 ($[C_{24}H_{27}N_{15}+H]^+$; calc. 526.2652).

2-Phenylpyrimidine-4,6-dicarboxaldehyde Methyl[6-(1-methylhydrazino)pyrimidin-4-yl]hydrazone Methyl{6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl}hydrazone (**12b**). As described for **12a**, with **11b** (200 mg, 0.433 mmol), **9b** (100 mg, 0.595 mmol), and EtOH/$CHCl_3$ 6:4 (50 ml) at 40°: **12b** (150 mg, 56%). Yellow solid. M.p. >250°. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.51–8.45 (*m*, 4 H); 8.23 (*d*, 1 H); 8.01 (*s*, 1 H); 7.91 (*s*, 1 H); 7.84–7.77 (*m*, 4 H); 7.68 (*s*, 1 H); 7.51–7.48 (*m*, 4 H); 7.14 (*t*, 1 H); 6.93 (*t*, 1 H); 6.61 (*s*, 1 H); 3.71 (*s*, 3 H); 3.68 (*s*, 3 H); 3.54 (*s*, 3 H); 3.00 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 165.2; 164.0; 162.8; 162.1; 162.0; 161.1; 159.9; 157.0; 156.4; 148.9; 137.8; 137.5; 136.1; 135.8; 134.5; 130.9; 128.7; 128.3; 122.8; 119.6; 107.7; 104.4; 88.8; 85.4; 39.6; 30.2; 29.9; 29.8. FAB-MS: 602.3 (100, $[M+H]^+$). HR-FAB-MS: 602.2960 ($[C_{30}H_{31}N_{15}+H]^+$; calc. 602.2965).

Pyrimidine-4,6-dicarboxaldehyde 4-[Methyl[6-[1-methyl-2-(pyridin-2-ylmethylene)hydrazino]pyrimidin-4-yl}hydrazone] 6,6′-[(Pyrimidine-4,6-diyl)bis(methylhydrazone)] (**13**). As described for **12a**, with **12a** (300 mg, 0.570 mmol), **14a** (120 mg, 0.882 mmol), and EtOH/$CHCl_3$ 5:5 (50 ml) at 45°: **13** (234 mg, 64%). Yellow solid. M.p. >300° (dec.). UV/VIS ($CHCl_3$): 309.0 (79800). IR (KBr): 1712*w*, 1590*s*, 1479*s*, 1401*m*, 1339*m*, 1190*m*, 1153*w*, 1075*m*, 1025*s*, 981*m*, 786*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 9.70 (*s*, 1 H); 9.21 (*s*, 1 H); 9.02 (*s*, 1 H); 8.62 (*s*, 1 H); 8.28–8.24 (*m*, 3 H); 8.06 (*s*, 1 H); 7.84 (*s*, 1 H); 7.71–7.65 (*m*, 2 H); 7.56 (*s*, 1 H); 7.51 (*s*, 1 H); 7.46 (*s*, 1 H); 7.34 (*s*, 1 H); 7.11 (*t*, 1 H); 6.82 (*t*, 1 H); 3.67 (*s*, 3 H); 3.61–3.52 (*m*, 12 H). ^{13}C-NMR ($CDCl_3$,

100 MHz): 191.7; 182.2; 163.0; 162.0; 161.9; 161.6; 161.5; 161.3; 159.7; 159.1; 156.7; 156.6; 156.3; 153.6; 149.0; 135.7; 135.6; 135.5; 133.2; 122.4; 119.4; 111.6; 109.4; 103.9; 90.4; 88.9; 30.2; 30.0; 28.9; 29.6. 2D-NMR (300 MHz): COSY, NOESY. FAB-MS: 644.4 (100, $[M+H]^+$). HR-FAB-MS: 644.2819 ($[C_{30}H_{29}N_{17}O+H]^+$; calc. 644.2819).

Pyrimidine-4,6-dicarboxaldehyde Methyl(pyridin-2-yl)hydrazone (**15**). To a soln. of **14a** (280 mg, 2.059 mmol) in EtOH (20 ml), cooled at −78°, **26a** (100 mg, 0.813 mmol) in EtOH (20 ml) was slowly added under magnetic stirring during 1 h. Then, the mixture was allowed to slowly warm to r.t. and was filtered. The filtrate was concentrated (1–1.5 ml) *in vacuo*, then MeCN (15 ml) was added. The precipitate was further purified by FC (Al_2O_3, $CHCl_3$, then $CHCl_3$/EtOH 97:3) to give the hydrate of aldehyde **15**, which was further dried overnight under vacuum at 35°: **15** (60 mg, 31%). Yellow solid. M.p. >150°. ^{1}H-NMR ($CDCl_3$, 300 MHz): 10.09 (*s*, 1 H); 9.46 (*s*, 1 H); 8.35 (*s*, 1 H); 8.28 (*d*, 1 H); 7.76 (*d*, 1 H); 7.70 (*t*, 1 H); 7.62 (*s*, 1 H); 6.95 (*t*, 1 H); 3.75 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 193.1; 164.5; 157.2; 156.6; 147.1; 138.0; 130.9; 117.8; 111.5; 110.7; 58.4; 30.3. 2D-NMR (300 MHz): COSY, NOESY. FAB-MS: 242.3 (100, $[M+H]^+$). HR-FAB-MS: 242.1041 ($[C_{12}H_{11}N_5O+H]^+$; calc. 242.1042).

Methyl 3,4,5-Trimethoxybenzenecarboximidate Hydrochloride (**17**). A cooled soln. of 3,4,5-trimethoxybenzonitrile (2 g, 51.7 mmol) in dry MeOH (120 ml) was stirred for 2 days at r.t. under an atmosphere of dry HCl. The soln. was concentrated and Et_2O added until precipitation was complete. The solid was isolated by vacuum filtration and washed with Et_2O: **17** (1.3 g, 68%). M.p. 179°. IR: 3052*w* (br.), 1702*w*, 1631*s*, 1262*m*. ^{1}H-NMR ((D_6)DMSO, 200 MHz): 7.42 (*s*, 2 H); 7.21 (*s*, 1 H); 4.23 (*s*, 3 H); 3.86 (*s*, 6 H); 3.71 (*s*, 3 H). ^{13}C-NMR ((D_6)DMSO, 50 MHz): 175.2; 173.3; 167.1; 152.3; 55.8; 26.6; 24.1; 23.1. EI-MS: 225.1 ($[M-HCl]^+$). Anal. calc. for $C_{11}H_{16}ClNO_4$: C 50.48, H 6.16, N 5.35; found: C 50.30, H 5.13, N 5.65.

3,4,5-Trimethoxybenzenecarboximidamide Hydrochloride (**18**). To a sat. soln. of dry ammonia in anh. MeOH (120 ml) was added **17** (5.00 g, 20.2 mmol), and the mixture was stirred at r.t. in a closed flask for 2 days. Then the soln. was concentrated, Et_2O was added and the precipitate filtered and washed with Et_2O: **18** (4.25 g, 85%). White powder. M.p. 228°. IR (KBr): 3350*m*, 1676*s*, 1420*s*. ^{1}H-NMR ((D_6)DMSO, 200 MHz): 7.32 (*s*, 2 H); 3.87 (*s*, 6 H); 3.75 (*s*, 3 H); 1.20 (*m*, 3 H). ^{13}C-NMR ((D_6)DMSO, 50 MHz): 164.7; 152.7; 122.3; 60.1; 56.2; 25.1. EI-MS: 210.2 ($[M-HCl]^+$). Anal. calc. for $C_2H_{15}ClN_2O_3 \cdot 0.4$ HCl: C 45.15, H 6.01, N 11.01; found: C 45.14, H 6.05, N 11.05.

2-(3,4,5-Trimethoxyphenyl)pyrimidine-4,6-diol (**19**). To a soln. of **18** (0.5 g, 2.02 mmol) and diethyl malonate (0.35 ml, 2.1 mmol) in anh. MeOH (2 ml) was added 30% MeONa/MeOH (1.1 ml). Then the milky soln. was heated to reflux for 24 h under Ar. After evaporation, the resulting paste was dissolved in H_2O and acidified to pH 1 and the white precipitate collected, washed with H_2O, and dried for 48 h under high vacuum at 40°: **3** (0.28 g, 41.6%). White solid. M.p. >250°. IR (KBr): 2600–2800*m*, 1621*s*, 1520*s*. ^{1}H-NMR ((D_6)DMSO, 200 MHz): 7.46 (*s*, 2 H); 5.30 (*s*, 1 H); 3.85 (*s*, 6 H); 3.72 (*s*, 3 H). ^{13}C-NMR ((D_6)DMSO, 50 MHz): 167.2; 156.7; 152.7; 140.4; 127.0; 88.1; 60.0; 56.0; 25.1. EI-MS: 278.2. Anal. calc. for $C_{13}H_{14}N_2O_5 \cdot 0.75$ H_2O: C 53.51, H 5.35, N 9.60; found: C 53.56, H 5.33, N 9.64.

4,6-Dimethyl-2-phenylpyrimidine (**21**). A mixture of 2-chloro-4,6-dimethylpyrimidine (**20**; 2 g, 14 mmol), phenylboronic acid (2.17 g, 14.2 mmol), $[Pd(PPh_3)_4]$ (200 mg), and K_3PO_4 (6.4 g, 30 mmol) was heated to reflux for 12 h in degassed toluene (20 ml). After cooling, the soln. was washed twice with H_2O and the org. phase dried ($MgSO_4$) and purified by FC (SiO_2, CH_2Cl_2/AcOEt 15:1): **21** (2.1 g, 80%). ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.41 (*m*, 2 H); 7.47 (*m*, 3 H); 6.12 (*s*, 1 H); 2.54 (*s*, 6 H).

2-(1-Methylhydrazino)-6-phenylpyridine (**26b**). To ice-cooled **25a** (10 g, 0.217 mol), 2-bromo-6-phenylpyridine (**24b**; 145 mg, 0.619 mmol) was slowly added. Then the mixture was refluxed under Ar during 1 h. The excess of **25a** was evaporated, the residue dissolved in $CHCl_3$ (10 ml), K_2CO_3 (150 mg, 1.087 mmol) added, and the suspension stirred for 10 min. The suspension was filtered and the filtrate evaporated: **26b** (120 mg, 97%). Yellowish oil, unstable in air, stored at low temp. under Ar. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.05 (*d*, 2 H); 7.56 (*t*, 1 H); 7.51–7.40 (*m*, 3 H); 7.13 (*d*, 1 H); 6.9 (*d*, 1 H); 4.15 (*s*, 2 H); 3.35 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 160.9; 154.7; 139.8; 137.9; 128.6; 128.5; 126.7; 109.4; 105.9; 41.0. FAB-MS: 200.1 (100, $[M+H]^+$). HR-FAB-MS: 200.1193 ($[C_{12}H_{13}N_3+H]^+$; calc. 200.1188).

2-(1-Hexylhydrazino)pyridine (**26c**). To ice-cooled **25b** (7 g, 60.345 mmol), **24a** (1.6 g, 10.256 mmol) was slowly added, and the mixture was heated for 3 h at 140° under Ar. Then the excess of **25b** was evaporated under high vacuum and the residue purified by FC (Al_2O_3, $CHCl_3$/hexane 7:3: **26c** (0.750 g, 38%). Yellowish oil, unstable in air, stored at low temp. under Ar. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.29 (*d*, 1 H); 7.38 (*t*, 1 H); 6.84 (*d*, 1 H); 6.50 (*t*, 1 H); 3.89 (*s*, 2 H); 3.56 (*t*, 2 H); 1.59 (*t*, 2 H); 1.41–1.25 (*m*, 6 H); 0.84 (*t*, 3 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 147.3; 136.8; 112.2; 106.8; 52.1; 31.6; 27.0; 26.5; 22.5; 13.9. EI-MS: 193.1 (M^+). FAB-MS: 194.1 (100, $[M+H]^+$). HR-FAB-MS: 194.1652 ($[C_{11}H_{19}N_3+H]^+$; calc. 194.1657).

2-[1-(Pyridin-2-yl)hydrazino]ethanol (**26d**). To ice-cooled **25c** (1 g, 13.158 mmol), **24a** (2 g, 12.658 mmol) was slowly added. Then the mixture was heated at 120° under Ar for 10 h. Purification by FC (Al_2O_3, $CHCl_3$, then $CHCl_3$/MeOH 93:7 gave **26d** (730 mg, 38%). Yellowish oil, unstable in air, stored at low temp. under Ar. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.03 (*d*, 1 H); 7.43 (*t*, 1 H); 6.96 (*d*, 1 H); 6.56 (*t*, 1 H); 4.15 (*s*, 3 H); 3.85 (*t*, 2 H); 3.72 (*t*, 2 H). ^{13}C-NMR ($CDCl_3$, 100 MHz): 158.7; 147.1; 146.8; 137.6; 113.3; 61.6; 55.6. EI-MS: 153.3 (33, M^+), 122.3 (100), 78.4 (95). FAB-MS: 154.0 (100, $[M+H]^+$). HR-FAB-MS: 154.0979 ($[C_7H_{11}N_3O+H]^+$; calc. 154.0980).

Crystal-Structure Analyses. The crystals were placed in oil, and a single crystal was selected, mounted on a glass fiber and placed in a low-temp. N_2 stream. The X-ray-diffraction data were collected on a *Nonius-Kappa-CCD* diffractometer with graphite monochromatized MoK_α radiation (λ 0.71071 Å), φ scans, by means of a 'φ scan' type scan mode. The structures were solved by direct methods and refined (based on F^2 with all independent data) by full-matrix least-squares methods (OpenMoleN package).

Crystal Structure of **1c**. A suitable crystal of **1c** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeOH (nonsolvent). Diffraction data were collected at 173 K. $C_{24}H_{22}N_8$, M_r 422.50. Yellow crystal, crystal size $0.10\times0.10\times0.08$ mm. Unit-cell parameters: $a=7.8112(1)$ Å, $b=24.7505(3)$ Å, $c=21.8993(4)$ Å, $\alpha=90°$, $\beta=90°(5)$, $\gamma=90°$; crystal system: orthorhombic; space group *Pbca*; $V=4233.8(1)$ Å^3; $F(000)=1776$; $Z=8$; calc. density $=1.33$ g·cm^{-3}; linear absorption coefficient $\mu=0.084$ mm^{-1}. Of 6360 reflections measured, 3364 reflections were unique ($I>3\,\sigma(I)$); 289 variables refined. The θ range for data collection was 2.5° – 29.11° with *hkl* limits 0 to 10, 0 to 29, and 0 to 33, resp. The final indices were $R=0.066$ and $R_w=0.071$, with a goodness-of-fit of 1.177. The largest peak in final difference was 0.525 eÅ^{-3}. Trans. min and max: 0.991 and 0.993, resp.

Crystal Structure of **2a**. A suitable crystal of **2a** was obtained by diffusion-recrystallization from CH_2Cl_2 (solvent)/MeCN (nonsolvent). Diffraction data were collected at 173 K. $C_{31}H_{32}Cl_2N_{16}=C_{30}H_{30}N_{16}\cdot CH_2Cl_2$, M_r 699.61. Yellow crystal, crystal size $0.12\times0.10\times0.08$ mm. Unit-cell parameters: $a=31.6897(5)$ Å, $b=10.4646(2)$ Å, $c=25.977(4)$ Å, $\alpha=90°$, $\beta=126.951°(5)$, $\gamma=90°$; crystal system: monoclinic; space group *C*12/*c* 1; $V=6783.7$ Å^3 (5); $F(000)=2912$; $Z=8$; calc. density $=1.37$ g·cm^{-3}; linear absorption coefficient $\mu=0.975$ m^{-1}. Of 17113 reflections measured, 3887 reflections were unique ($I>3\sigma(I)$); 442 variables refined. The θ range for data collection was 2.5° – 30.06° with *hkl* limits −44 to 44, −13 to 14, and −36 to 35, resp. The final indices were $R=0.058$ and $R_w=0.068$, with a goodness-of-fit of 1.031. The largest peak in final difference was 0.375 eÅ^{-3}. Trans. min and max: 0.971 and 0.981, resp.

Crystal Structure of **2c**. A suitable crystal of **2c** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeOH (nonsolvent). Diffraction data were collected at 173 K. $C_{48}H_{42}N_{16}$, M_r 842.98. Yellow crystal, crystal size $0.14\times0.12\times0.08$ mm. Unit-cell parameters: $a=8.5901(1)$ Å, $b=23.3589(2)$ Å, $c=42.3853(4)$ Å, $\alpha=90°$, $\beta=90°(5)$, $\gamma=90°$; crystal system: orthorhombic; space group *Pbca*; $V=8504.8(1)$ Å^3; $F(000)=3536$; $Z=8$; calc. density $=1.32$ g·cm^{-3}; linear absorption coefficient $\mu=0.084$ mm^{-1}. Of 24014 reflections measured, 4553 reflections were unique ($I>3\,\sigma(I)$); 577 refined variables. The θ range for data collection was 2.5° – 30.02° with *hkl* limits −12 to 12, −32 to 32, and −59 to 59, resp. The final indices were $R=0.042$ and $R_w=0.062$, with a goodness-of-fit of 1.133. The largest peak in final difference was 0.386 eÅ^{-3}. Trans. min and max: 0.988 and 0.993, resp.

Crystal Structure of **3a**. A suitable crystal of **3a** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeOH (nonsolvent). Diffraction data were collected at 173 K. $C_{43}H_{44}Cl_2N_{24}=C_{42}H_{42}N_{24}\cdot CH_2Cl_2$, M_r 967.90. Yellow crystal, crystal size $0.12\times0.10\times0.08$ mm. Unit-cell parameters: $a=20.5729(6)$ Å, $b=16.6524(6)$ Å, $c=14.7563(5)$ Å, $\alpha=90°$, $\beta=106.062°(5)$, $\gamma=90°$; crystal system: monoclinic; space group *C*12/*c* 1; $V=4858.0$ Å^3 (3); $F(000)=2016$; $Z=4$; calc. density $=1.32$ g·cm^{-3}; linear absorption coefficient $\mu=0.193$ mm^{-1}. Of 10990 reflections measured, 2381 reflections were unique ($I>3\,\sigma(I)$); 326 variables refined. The θ range for data collection was 2.5° – 29.20° with *hkl* limits −28 to 28, −22 to 19, and −20 to 20, resp. The final indices were $R=0.099$ and $R_w=0.128$, with a goodness-of-fit of 1.109. The largest peak in final difference was 0.532 eÅ^{-3}. Trans. min and max: 0.977 and 0.985, resp.

Crystal Structure of **3c**. A suitable crystal of **3c** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeOH (nonsolvent). Diffraction data were collected at 173 K. $C_{146}H_{129}Cl_3N_{48}O=2(C_{72}H_{62}N_{24})\cdot CHCl_3\cdot MeOH$, M_r 2678.34. Colorless crystal, crystal size $0.14\times0.10\times0.08$ mm. Unit-cell parameters: $a=11.8926(2)$ Å, $b=16.3930(2)$ Å, $c=19.9753(3)$ Å, $\alpha=105.840(5)°$, $\beta=102.776°(5)$, $\gamma=98.848(5)°$; crystal system: triclinic; space group $P-1$; $V=3557.20(18)$ Å^3; $F(000)=1400$; $Z=2$; calc. density $=1.25$ g·cm^{-3}; linear absorption coefficient $\mu=0.134$ mm^{-1}. Of 28392 reflections measured, 8329 reflections were unique ($I>3\,\sigma(I)$); 910 refined variables. The θ range for data collection was 2.5° – 30.06° with *hkl* limits −16 to 14, −19 to 23, and −28 to 27, resp. The final indices were $R=0.106$ and $R_w=0.147$, with a goodness-of-fit of 1.200. The largest peak in final difference was 0.973 eÅ^{-3}. Trans. min and max: 0.981 and 0.989, resp.

Crystal Structure of **5**. A suitable crystal of **5** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeOH (nonsolvent). Diffraction data were collected at 173 K. $C_{70}H_{71}Cl_6N_{41} = C_{66}H_{66}N_{40} \cdot 2\ CHCl_3 \cdot$ MeCN, M_r 1699.33. Colorless crystal, crystal size $0.10 \times 0.08 \times 0.08$ mm. Unit-cell parameters: $a = 12.8281(3)$ Å, $b = 17.2593(6)$ Å, $c = 18.4109(5)$ Å, $\alpha = 87.701°(5)$, $\beta = 79.546°(5)$, $\gamma = 78.697°(5)$; crystal system: triclinic; space group $P-1$; $V = 3930.8$ Å^3 (2); $F(000) = 1754$; $Z = 2$; calc. density = 1.43 g·cm^{-3}; linear absorption coefficient $\mu = 0.291$ mm^{-1}. Of 19688 reflections measured, 6898 reflections were unique ($l > 3\ \sigma(l)$); 1054 variables refined. The θ range for data collection was 2.5° – 28.78° with *hkl* limits 0 to 17, − 22 to 23, and − 24 to 24, resp. The final indices were $R = 0.136$ and $R_w = 0.157$, with a goodness-of-fit of 1.473. The largest peak in final difference was 0.912 eÅ^{-3}. Trans. min and max: 0.6607 and 1.1084, resp.

Crystal Structure of **6**. A suitable crystal of **6** was obtained by diffusion-recrystallization from CH_2Cl_2/$CHCl_3$ 1:1 (solvent mixture) and MeCN (nonsolvent). Diffraction data were collected at 173 K. $C_{24}H_{24}N_{12}$, M_r 480.54. Yellow crystal, crystal size $0.16 \times 0.10 \times 0.08$ mm. Unit-cell parameters: $a = 10.7540(3)$ Å, $b = 11.5938(4)$ Å, $c = 11.7085(3)$ Å, $\alpha = 112.259°(5)$, $\beta = 110.617°(5)$, $\gamma = 110.669°(5)$; crystal system: triclinic; space group $P-1$; $V = 1165.59$ Å^3 (12); $F(000) = 504$; $Z = 2$; calc. density = 1.37 g·cm^{-3}; linear absorption coefficient $\mu = 0.090$ mm^{-1}. Of 9564 reflections measured, 3721 reflections were unique ($l > 3\ \sigma(l)$); 325 variables refined. The θ range for data collection was 2.5° – 29.99° with *hkl* limits − 14 to 15, − 16 to 15, and − 15 to 16, resp. The final indices were $R = 0.053$ and $R_w = 0.082$, with a goodness-of-fit of 1.413. The largest peak in final difference was 0.436 eÅ^{-3}.

Crystal Structure of **7**. A suitable crystal of **7** was obtained by diffusion-recrystallization from $CHCl_3$ (solvent)/MeCN (nonsolvent). Diffraction data were collected at 173 K. $C_{32}H_{32}Cl_6N_{16} = C_{30}H_{30}N_{16} \cdot 2\ CHCl_3$, M_r 853.44. Colorless crystal, crystal size $0.10 \times 0.08 \times 0.06$ mm. Unit-cell parameters: $a = 11.4802(2)$ Å, $b = 13.4750(2)$ Å, $c = 13.7730(3)$ Å, $\alpha = 110.805°(5)$, $\beta = 96.450°(5)$, $\gamma = 101.830°(5)$; crystal system: triclinic; space group $P-1$; $V = 1909.06$ Å^3 (11); $F(000) = 876$; $Z = 2$; calc. density = 1.48 g·cm^{-3}; linear absorption coefficient $\mu = 0.500$ mm^{-1}. Of 15488 reflections measured, 4278 reflections were unique ($l > 3\ \sigma(l)$); 487 variables refined. The θ range for data collection was 2.5° – 30.07° with *hkl* limits − 16 to 16, − 18 to 18, and − 12 to 19, resp. The final indices were $R = 0.104$ and $R_w = 0.113$, with a goodness-of-fit of 1.020. The largest peak in final difference was 0.977 eÅ^{-3}. Trans. min and max: 0.950 and 0.970, resp.

Crystallographic data for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as depositions Nos. CCDC-205254 (**1c**), CCDC-205249 (**2a**), CCDC-205255 (**2c**), CCDC-205251 (**3a**), CCDC-205253 (**3c**), CCDC-205252 (**5**), CCDC-205248 (**6**), and CCDC-205250 (**7**). Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB IEZ UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

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