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Synthesis and noncovalent polymerization of self-complementary hydrogen-bonding supramolecular synthons: *N,N′*-disubstituted 4,6-diamino-pyrimidin-2(1*H*)-ones†

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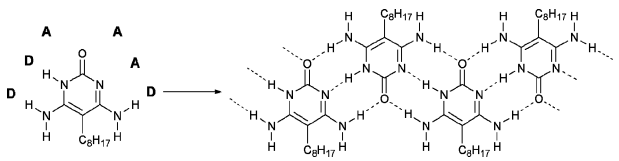
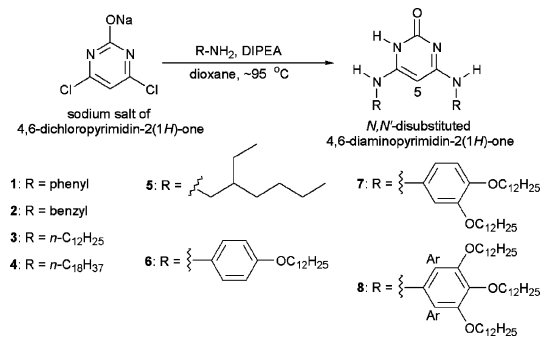
A series of self-complementary *N,N′*-disubstituted 4,6-diamino-pyrimidin-2(1*H*)-ones self-assemble in organic solvents to form a robust and linear supramolecular polymer network *via* DDA·AAD hydrogen-bonding.

Noncovalent association of small molecules into well-ordered molecular arrays is a versatile tool for creating optoelectronic devices.[1] Because of the high selectivity, directionality and reversibility of hydrogen-bonds as intermolecular glue, development of hydrogen-bonding supramolecular synthons[2] that can self-assemble with long-range ordering is the most reliable approach to obtain scaffolds for the ordered alignment of functional entities. At the same time, such supramolecular synthons are required for synthetic accessibility in functionalization. Self-complementary 5-monosubstituted 4,6-diaminopyrimidin-2(1*H*)-one, comprising G(DDA) and C(AAD) nonsymmetrical hydrogen-bonding surfaces, reported by Lehn *et al.*, is a potentially useful supramolecular synthon and exhibits linear molecular arrays based on intermolecular DDA·AAD hydrogen-bonding networks in its X-ray crystal structure (Scheme 1).[3] Though the poor solubility of this compound is an unequivocal sign of the formation of highly polymeric assemblies in the solid state, at the same time, it hampers solution studies of its self-assembly in which association dynamics strongly relies on the strength of hydrogen-bonding interactions. Furthermore, functionalization of 5-monosubstituted pyrimidinone is synthetically rather difficult. We report herein the facile synthesis of *N,N′*-disubstituted 4,6-diaminopyrimidin-2(1*H*)-ones (Scheme 2) and their self-assemblies in organic media. Great advantages of GC-hybrid self-complementary synthons are highlighted by the strong binding constant of the DDA·AAD hydrogen-bonding motif



Scheme 1 Self-aggregation of 5-octyl-4,6-diaminopyrimidin-2-(1*H*)-one.



Scheme 2 Synthesis of *N,N′*-disubstituted 4,6-pyrimidin-2(1*H*)-ones.

† Electronic Supplementary Information (ESI) available: Synthesis and characterization data of **1–8**, FAB-MS spectra of **1–4**. See http://www.rsc.org/suppdata/cc/b4/b401132e/

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(in $CHCl_3$, K_{assoc} = 10^4 M^{-1})[4] in addition to its well-programmed molecular structure to assemble selectively into the linear polymeric architecture in contrast to well-known coaggregates between melamines and barbiturates (or cyanurates).[5]

Pyrimidinone **1–8** are substituted at the two exocyclic amino groups. From the practical point of view, substitution at these two amino groups is advantageous over 5-monosubstituted pyrimidinone derivatives in terms of achieving dense functionalization of a polymeric structure. All pyrimidinone derivatives **1–8** were prepared *via* the reaction of the sodium salt of 4,6-dichloropyrimidin-2(1*H*)-one[6] with 4 equiv. of the corresponding aliphatic or aromatic amines as solubilizing chains in dioxane at 80–105 °C. In all reactions, insoluble products were precipitated from the reaction mixture with cooling to room temperature (rt). All precipitated products were found to be almost pure **1–8** without further purification as characterized by ^{1}H NMR, FAB-MS and elemental analysis. This synthetic procedure facilitates the introduction of chemically labile functional groups such as dyes because it does not require the cyclization process for creating pyrimidine rings by the action of strong base as in the preparation of 5-monosubstituted 4,6-diaminopyrimidin-2(1*H*)-ones.[3]

Compounds **1–4** were sparingly soluble in common organic solvents even upon refluxing in hydrogen-bond breaking DMSO and DMF. The insolubility of **3** and **4** despite the presence of long lipophilic chains is remarkable, implying the formation of highly polymeric assemblies based on strong DDA·AAD hydrogen-bonding. Addition of 10 equiv. of trifluoroacetic acid (TFA), a hydrogen-bond rupturing reagent which protonates the basic nitrogen atoms, to these compounds suspended in $CHCl_3$ dramatically promoted dissolution to give homogeneous solutions. FAB-MS spectra measured for these acidic solution gave peaks corresponding to monomeric ($[M + H]^+$), dimeric ($[2M + H]^+$) and trimeric species ($[3M + H]^+$), indicating self-association of these compounds (see ESI†).

In sharp contrast to **1–4**, pyrimidinones **5–8** were moderately soluble in $CHCl_3$ (at rt), cyclohexane (with heating) and other nonpolar solvents. The branching effect[7] is remarkable as it renders **5** soluble even in the least polar cyclohexane at 60 °C over 200 mM. Despite the high insolubilities of **3** and **4**, pyrimidinone **6** dissolved in cyclohexane at 60 °C (over 150 mM). The significant increase in solubility of **5–8** can be explained by intermolecular steric repulsion between the bulky substituents in polymeric structures, affording considerable perturbation to their flatness, and thereby increasing their solubilities.[8]

To establish the formation of polymeric assemblies in solution, self-assembly of **5–8** in $CDCl_3$ was assessed by ^{1}H NMR spectroscopy. As exemplified by the spectrum of **8** (5 mM) in $CDCl_3$ (Fig. 1a), all proton resonances of **5–8** in $CDCl_3$ were highly broadened, indicating formation of polymeric structures. With the dimerization constant K_D = 10^4 M^{-1} for the GC complex,[4] the mean degree of polymerization can be estimated as 15 at this concentration in $CDCl_3$.[9] Addition of hydrogen-bond breaking DMSO (19 vol%) did induce sharpening and chemical shift changes for all proton signals (Fig. 1b), while further addition did not afford a monomeric spectrum until precipitation occurred (over 20 vol%). This again indicates the presence of a robust supramolecular polymer based on the DDA·AAD hydrogen-bonding motif.

Addition of a small amount of TFA resulted in the sharp spectrum of the molecularly dissolved state (Fig. 1c).

One of the impressive aspects of supramolecular polymers is rupture of polymeric chains by the addition of monofunctional chain stoppers.[9] Thus, chain stopper **9** was synthesized and used for an end-capping experiment of supramolecular polymer $\mathbf{8}_n$. As shown in Fig. 2, ^{1}H NMR titration of $\mathbf{8}_n$ in $CDCl_3$ (5 mM) with **9** resulted in gradual sharpening of the signals of aromatic protons (Ar-H) and ether CH_2 protons of **8**, which is a clear sign of a decrease in the degree of polymerization. A remarkable high-field shift was observed for the signals of the pyrimidinone ring proton of **8** (5-H) with rupture of polymeric chains. The large low-field shift ($\Delta\delta$ = 0.48) of this proton of **8** in the polymeric state may come from a deshielding effect of the tridodecyloxyphenyl moieties, conformation of which was restricted by hydrogen-bonding of the exocyclic amino groups in a highly polymeric state.

Since the macroscopic morphology of supramolecular polymers can be well-reflected by the gelation behavior in organic solvents, we examined the gelling capability of soluble compounds **5–8** in chloroform, toluene and cyclohexane.‡ All compounds in chloroform gave gel-like highly viscous fluids at high concentrations over 150 mM. For example, **8** completely gelated chloroform at 280 mM. This concentration corresponds to a mean degree of polymerization of 106 (total molar mass 2×10^5 g mol^{-1}, chain length *ca.* 56 nm based on molecular modeling). **5** gelated cyclohexane and toluene at relatively high concentrations (120 mM) whereas **6** and **7** in toluene and cyclohexane precipitated upon cooling. **8** showed moderate gelation ability in toluene and cyclohexane, giving transparent gels. The minimum concentration for gelation was 40 mM in cyclohexane and 80 mM in toluene. Relatively low gelation abilities of **5–8** in nonpolar organic solvents despite their high polymerizabilities indicate that their polymeric structures are macroscopically rigid and linear, which is unfavorable for the formation of three-dimensional entangled networks and thereby contain less void volume than flexible fibrous assemblies.

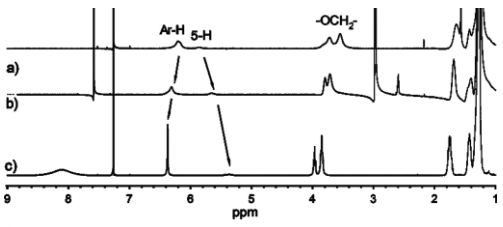

Fig. 1 ^{1}H NMR spectra of **8** (5 mM) in $CDCl_3$ with no hydrogen-bond rupturing reagent (a), with 20 vol% DMSO (b) and with 15 equiv. of TFA (c). Annotations refer to Scheme 2.

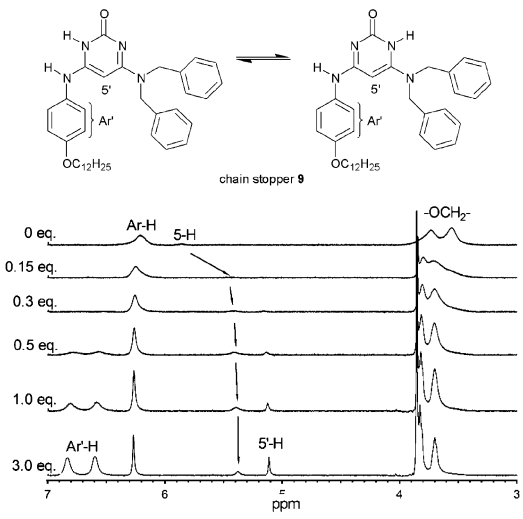

Fig. 2 ^{1}H NMR titration of **8** (5 mM) with chain stopper **9** in $CDCl_3$. Annotations refer to Scheme 2.

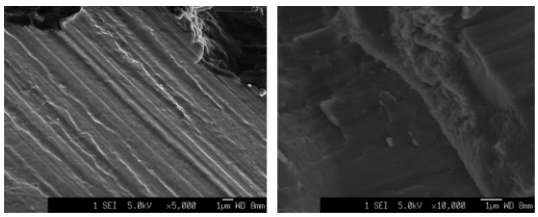

Fig. 3 SEM images of a dried gel of **8** from cyclohexane. Scale bar is 1 μm. Right image shows the cross-section of lamellar structures.

Scanning electron microscopy (SEM) observation of the dried gel of **8** from cyclohexane showed omnipresence of the long-range lamellar structures (Fig. 3), which must be hierarchically constructed from a two-dimentional linear array of **8**. This is in line with the low-gelation abilities of **8** described above.

In conclusion, we have demonstrated the supramolecular polymerizations of self-complementary 4,6-diaminopyrimidin-2(1*H*)-ones in organic solvents. The resulting supramolecular polymers showed remarkable robustness and macroscopic rigidity and linearity. Furthermore, the present supramolecular synthons can be readily functionalized by changing the substituents at the amino groups, allowing alignment of various functional units with long-range ordering. We are currently introducing various optically and electronically active substituents into the present supramolecular synthons and investigating their photoresponsive and electron conducting properties.

Notes and references

‡ Gelation ability was estimated as follows. The sample in an appropriate organic solvent was heated in a sealed vial (Φ = 16.5 mm) to be dissolved completely, and the resulting homogeneous solution was cooled to rt. Gelation was checked by the inverse fluid method.

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