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Creating nanocavities of tunable sizes: Hollow helices

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Creating nanocavities of tunable sizes: Hollow helices

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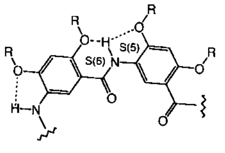
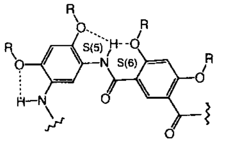
A general strategy for creating nanocavities with tunable sizes based on the folding of unnatural oligomers is presented. The backbones of these oligomers are rigidified by localized, three-center intramolecular hydrogen bonds, which lead to well-defined hollow helical conformations. Changing the curvature of the oligomer backbone leads to the adjustment of the interior cavity size. Helices with interior cavities of 10 Å to >30 Å across, the largest thus far formed by the folding of unnatural foldamers, are generated. Cavities of these sizes are usually seen at the tertiary and quaternary structural levels of proteins. The ability to tune molecular dimensions without altering the underlying topology is seen in few natural and unnatural foldamer systems.

Based on the folding of biopolymers, Nature has developed astonishingly efficient and sophisticated strategies for generating various nanostructures. Of particular interests is the availability of a wide variety of nanosized cavities and holes that are responsible for numerous biological processes and functions. In recent years there has been intense interest in developing folding oligomers and polymers (foldamers) with unnatural backbones that adopt well-defined structures (1–3), which may eventually lead to protein-like molecular objects with sizes in the nanometer range. Many foldamer systems have been described (4–16). Despite the progress made so far, the foldamer field is still in its infancy. One daunting challenge involves the design of foldamers with cavities and holes of tunable sizes in the nanometer range, the realization of which will have far-reaching significance for not only fundamental understanding but also important applications. While cavities and holes are mostly seen at the tertiary and quaternary structural levels of biopolymers, almost all foldamers reported so far fold into secondary structures. In this article we describe a general strategy for designing folded structures that combine the features of both secondary and tertiary (or quaternary) structures. Nanosized cavities are generated by enforcing stably folded helical structures. In addition, by adjusting the curvature of the corresponding backbones, the interior diameters of these hollow helices are easily tuned. This tunability is seen in few natural or unnatural folding systems. Thus, helices with hydrophilic interior cavities of ~10 Å and >30 Å across result, yielding cavities of tunable sizes and properties. Many novel properties may emerge given, the tunable and distinct cavities associated with the corresponding folding molecules, and numerous applications in catalysis, separation, molecular recognition, and transportation can be envisioned. Phenomena associated with nanodimensions that lately have attracted intense interest and have been probed by using the highly hydrophobic carbon nanotubes (17, 18) can also be investigated on the basis of the hydrophilic cavities of these hollow helices.

Our design is based on oligoamides represented by the general structures **1a** and **1b**. The backbone of these oligomers consists of benzene rings linked by localized, intramolecularly hydrogen-bonded amide groups. On each of the benzene rings, the two amide linkages can be placed *meta* to each other (*m*-residue), leading to backbones consisting of *m*-residues (*m*-backbones, **1a**), or with some of the residues, the two amide groups can be placed in a *para* geometry (*p*-residue), leading to backbones consisting of *m*- and *p*-residues (*mp*-backbones, **1b**).



1a



1b

Our previous studies have demonstrated that short oligomers with *m*-backbones adopt a well-defined crescent conformation (12, 19, 20). Our results indicated that the three-center hydrogen-bonding system, consisting of the S(5) and S(6) type (21) hydrogen-bonded rings, was particularly stable in the solid state and in solution (19, 20). It persisted in chloroform, the highly polar dimethyl sulfoxide (DMSO), and even in water (unpublished data), and this structure was confirmed by NMR, IR, and x-ray crystallographic studies on short oligomers. Extending the crescent backbones may lead to helical conformations.

Materials and Methods

Compounds. All compounds described herein gave satisfactory NMR and electrospray ionization (ESI) MS results consistent with their structures. The short oligomer intermediates were prepared by iterative coupling steps based on similar procedures described before (12).

Compound 2a. To a solution of 4,6-bis{2-[2-(2-methoxyethoxy)-ethoxy]ethoxy}-1,3-benzenedicarboxylic acid (0.049 g, 0.10 mmol) and tetramer amine **4a** was added *N,N*-diisopropylethylamine (1 ml), followed by slow addition of *O*-(7-azabenzotriazol-1-yl)-*N,N,N′,N′*-tetramethyluronium hexafluorophosphate (0.076 g, 0.20 mmol) in dimethylformamide (DMF; 1 ml) during 10 min at 50°C under nitrogen atmosphere. The mixture was changed into solution, which was stirred overnight. The precipitate from the solution at −20°C was collected and washed with cold DMF and ethyl acetate to give pure **2a** as a solid (0.093 g, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 2H), 10.05 (s, 2H), 9.77 (s, 2H), 9.62 (s, 2H), 9.22 (s, 2H), 9.10 (s, 2H), 8.95 (s, 1H), 8.91 (s, 2H), 8.55 (s, 2H), 6.76 (d, 2H, J = 7.0 Hz), 6.72 (d, 2H, J = 7.0 Hz), 6.58 (s, 1H), 6.52 (br, 4H), 6.45 (s, 2H), 4.38(br, 4H), 4.26 (br, 8H), 3.94–4.04 (m, 40H),

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Abbreviations: ESI, electrospray ionization; DMF, dimethylformamide; 1D and 2D, one- and two-dimensional; NOESY, nuclear Overhauser and exchange spectroscopy; NOE, nuclear Overhauser enhancement.

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