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Tetrameric octi(*p*-phenylene) self-assemblies in aqueous solution: proof of principle of a novel suprastructural motif

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Abstract

A general supramolecular energy minimum has been predicted for tetrameric 'pinwheels', known as smallest units of herringbone-type suprastructures in H-aggregates and crystals of aromatic chromophores. As a proof of principle, we herein describe octi(*p*-phenylene)s that quantitatively self-assemble into novel tetrameric supramolecules in aqueous solution. © 1999 Elsevier Science Ltd. All rights reserved.

Although "...it appears to be reasonable that the 'pinwheel' unit may be a general supramolecular energy minimum for a variety of aromatics and conjugated compounds...",[1] the verified existence of single pinwheels has so far been restricted to anisotropic environments[1–3] because of their tendency to self-assemble into herringbone lattices to yield H-aggregates[1–3] or crystals[4] (Fig. 1). To design stable self-assembled tetrameric arene arrays for isotropic media, we considered pinwheels as high energy intermediates of the H-aggregation of arenes that, much alike intermediates of ordinary chemical reactions, could be isolated if the subsequent transformation could be inhibited by either increased relative activation or product energy. Here, we report the design and synthesis of tetrameric supramolecular arene arrays **1**^{4} that are surrounded by amphiphilic, anionic[5] Glu-Leu-Glu-residues to resist H-aggregation (Fig. 1), while spontaneous and quantitative self-assembly of monomeric octi(*p*-phenylene) **1** into tetramer **1**^{4} is governed by multiple, presumably edge-to-face π,π-interactions inbetween the entropy-minimized (i.e., 'preorganized') rigid-rod scaffolds (Fig. 2).

Octi(*p*-phenylene) **1** was synthesized by coupling H-Glu(*t*-Bu)-Leu-Glu(*t*-Bu)-NH_2 (prepared by conventional solution-state peptide synthesis) with the previously described[6] octaacid **2** (PyBOP, Hünig's base, DMF, 3 h, rt, 70%) followed by deprotection of **3** with TFA (quantitative, Fig. 2).[7] Quantitative self-assembly of **1** (calculated: 4,166) into tetramer **1**^{4} (calculated: 16,664; found: 16,716±700) was fully corroborated by size-exclusion chromatography in a saline phosphate buffer, pH 6.4, with standard protein calibration (Fig. 2).

The spectroscopic properties of tetramer **1**^{4} were intriguingly indistinct. In its ^{1}H NMR 500 MHz spectrum, broadening of the hardly visible arene- and the slightly upfield shifted Leu-resonances

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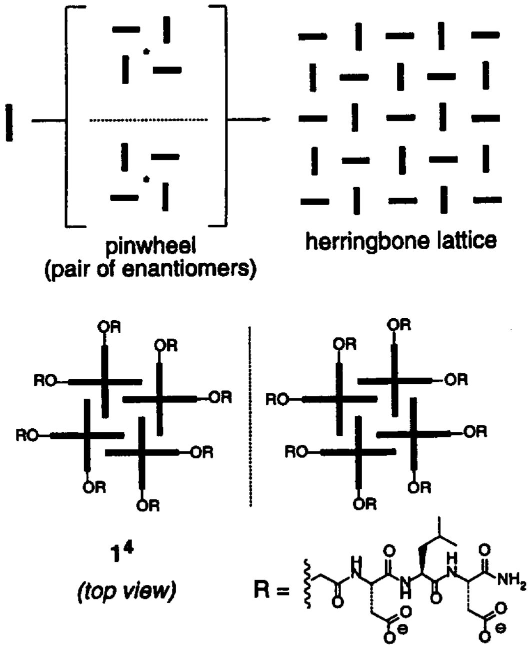
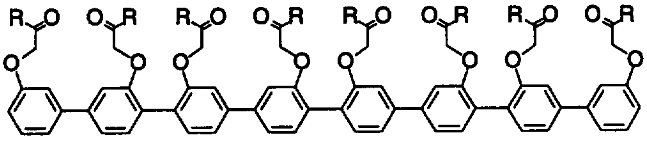


Figure 1.



2: R = OH
3: R = Glu(*t*Bu)-Leu-Glu(*t*Bu)-NH2
1: R = Glu-Leu-Glu-NH$_2$

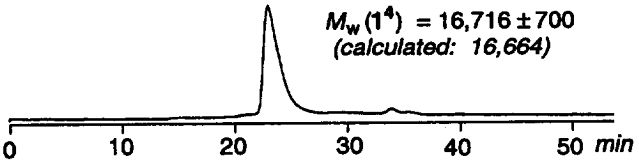


Figure 2.

contrasted sharply to the perfectly resolved signals for the random coil-type[8] Glu-residues at the surface of the self-assembly. Compared to that of monomeric **1**, the absorption of the ^{1}L transitions of **1**^{4} at 314 nm was about 3 nm blue-shifted as expected.[3,9] In light of the additional central chiral axis of pinwheels (Fig. 1, *), the absence of distinct circular dichroism Cotton effects for the ^{1}L transitions of **1**^{4} was of interest concerning the otherwise obscure exact structure of the arene array itself. Namely, it is most consistent with arene–arene torsion angles in tetramer **1**^{4} that alternate between 90° (for 2,2′- and 3,3′-substitution) and 0° (possible for 3,3′-substitution only) with inversion of pinwheel helicity by each torsion angle of 90°, because the resulting arene array per se would be achiral with respect to its central chiral axis (Fig. 1, **1**^{4} and *).[3]

In summary, we have described octi(*p*-phenylene)s that self-assemble into tetramers in aqueous solution. Quantitative self-assembly and stability to dilution implies general usefulness of this novel suprastructural motif for supramolecular design and synthesis.

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