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Helix *versus* zig-zag: control of supramolecular topology *via* carboxylic acid conformations in *ortho*-substituted phenyl amines

Jason E. Field and D. Venkataraman*

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts, USA 01003.
E-mail: dv@chem.umass.edu; Fax: +1-413-545-4490; Tel: +1-413-545-2028

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***ortho*-Substituted phenyl amines form supramolecular helices or zig-zag structures, depending on the conformation of the carboxylic acid substituents — which can be controlled by an intramolecular hydrogen-bonding interaction.**

Of all of nature's structures, there is arguably none more beautiful or widely scrutinized than the helix. Chemists have been attempting to mimic the helical motif in supramolecular assemblies in order to achieve functional materials.[1,2] With the development of crystal engineering,[3] chemists have identified a large number of intermolecular interactions to assemble targeted supramolecular motifs. Hydrogen-bonding is often applied in this regard due to the strength, directionality, and specificity of the interaction,[4] as well as its ubiquitous presence in naturally occurring assemblies. The major challenge that chemists face in creating predictable supramolecular assemblies from small molecules is to decipher nature's hierarchy of molecular interactions. It was our goal to manipulate an intramolecular interaction in order to control the conformation of an intermolecular interaction and thus provide a route to a predictable solid-state motif.[5] In this paper, we report an *ortho*-substituted phenyl amine that can form a hydrogen-bonded, crystalline, supramolecular helix. Furthermore, the conformation of the intermolecular hydrogen-bonds, and thus the overall structure, can be controlled through an intramolecular hydrogen-bond interaction.

There is some precedence to using the directionality of hydrogen-bonds to control supermolecular structure. For example, Wuest and co-workers have utilized symmetric and asymmetric dipyridones to control dimerization *versus* extended structure formation.[6] Our goal was to takes this idea one step further by controlling the conformation of a carboxylic acid hydrogen-bond synthon using an intramolecular interaction.[7] Fig. 1 shows three possible packing motifs of a bis(benzoic acid) system. Motif I is composed of two atropisomers and results in a zig-zag structure. Motifs II and III contain only a single atropisomer assembled as a trigonal coil and a circular helix respectively. The packing motifs available to this system are further limited by the three possible conformations of the carboxylic acids. The two symmetric conformations, with the carbonyls pointing in opposing directions, can only pack in motifs I or II due to the allowed intermolecular hydrogen bonding. In contrast, the asymmetric conformation, with the carbonyls both pointing in the same direction, can potentially pack in any of the three motifs. We set out to synthesize a series of bis(benzoic acids) with bridging groups that can form intramolecular hydrogen-bonds with the carboxylic acid groups, thereby controlling their conformations and thus the overall supramolecular motif.

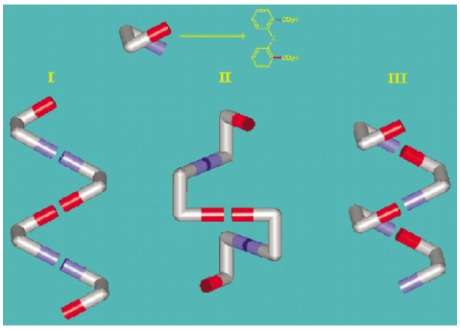
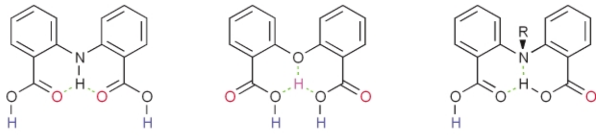


Fig. 1 The three possible packing motifs of a bridged bis(benzoic acid) system. X = bridging group. Motif I is racemic, motif II and III are composed of a single atropisomer.

Molecule **1** (Fig. 2) was synthesized through a novel copper-catalyzed coupling of methyl anthranilate and methyl-2-iodobenzoate which was developed by our group.[8] Subsequent base hydrolysis and recrystallization from ethanol gave **1**† as large yellow crystals. The resulting solid-state structure was obtained from single crystal X-ray diffraction and is shown in Fig. 3a. This structure shows that the intramolecular hydrogen-bonding of the secondary amine to the acid carbonyls serves to fix the conformation of the intermolecular hydrogen-bonds, which in turn gives rise to an overall zig-zag motif (I). It is important to note that this is not a helical structure, as the hydrogen-bonds are bisected by an imaginary central axis rather than coiled around it. We hypothesize that motif II is less favoured than motif I due to inefficient packing between stacks.



1 2 3

Fig. 2 The control of carboxylic acid conformations of **1**, **2**, and **3** (R = Phenyl) by internal hydrogen-bonding (green dashed). Intermolecular hydrogen-bond donors (blue) and acceptors (red); disordered hydrogen (magenta).

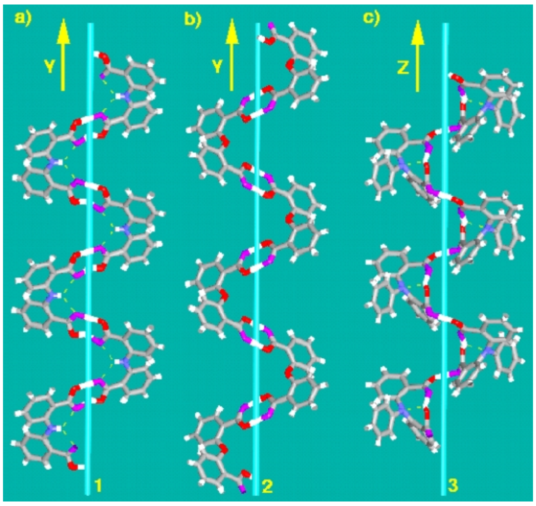


Fig. 3 The supramolecular structures of a) **1**, b) **2**, and c) **3** from single crystal X-ray diffraction. Carboxylic hydrogen bonds are connected for clarity. Internal hydrogen bonds (yellow dashed lines); oxygen (red), carbonyl oxygen (purple), nitrogen (blue), carbon (grey), hydrogen (white), imaginary axis (light blue) parallel to the specified crystallographic axis.

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To test our ability to control the carboxylic acid conformation, we synthesized **2** using a copper-catalyzed ether coupling of *o*-methylphenol and *o*-iodotoluene, previously reported by our group,[9] followed by oxidation with $KMnO_4$.[10] We hypothesized that the ether linkage would hydrogen-bond with one of the acidic hydrogens, resulting in the asymmetric conformation. Unfortunately, single crystal X-ray diffraction of **2**‡ (Fig. 3b) reveals that both carbonyls are facing in the same direction, resulting in a similar zig-zag structure as seen in **1**, except the conformation of the carboxylic acids are completely reversed. We hypothesize that the carboxyl hydrogens are slightly disordered such that one occupies the three-oxygen cavity for some percentage of time in the solid-state (Fig. 2),[11] thus providing stabilization for this conformation.

In order to achieve the desired assymmetric conformation, we synthesized **3** through an Ullmann coupling,§ followed by simple base hydrolysis and recrystallization from a water–acetone mixture. Single crystal X-ray diffraction shows that **3**¶ obtains an asymmetric conformation except the intermolecular hydrogen bonds are not dimeric. This is due to the internal hydrogen-bonds between the two carboxylic acids as well as the tertiary amine (Fig. 2). Moreover, **3** is observed to self-assemble into a supramolecular helix (Fig. 3c) as predicted by packing motif III. It should be noted that both the right-handed and left-handed helices are present in the unit cell. It is also important to note that solvent water does not interfere in the assembly of this helical structure, a common problem in supramolecular chemistry due to competition by the protic solvent for hydrogen bonds.[12]

As discussed previously, motif II is less favoured due to inefficient inter-stack packing, but it also forms a more rigid and a less efficient coil (more residues per length) than motif III. More difficult to explain is the absence of the zig-zag motif (I), which facilitates packing between stacks. The angle between the planes of the two benzoic acid rings are approximately 44°, 66°, and 81° corresponding to compounds **1**, **2**, and **3**, respectively. The more open angle of **3**, combined with its bonding conformation, may give rise to the helical assembly over the zig-zag structure. It is also possible that the bulk of the additional phenyl group in **3** is better accommodated by the helical motif in this case.

In summary, we have reported a novel molecular system in which the conformation of the intermolecular hydrogen-bonding, and thus the supramolecular structure, can be controlled through an internal hydrogen-bond. This work is an example of a rational design approach for assembling predictable molecular architectures that may potentially lead to functional materials with interesting solid-state properties.[13] The triphenylamine moiety may also assist in the development of such materials.[14] Studies are under way to determine if these molecules aggregate in the solution phase.

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Notes and references

† *Crystal data* for **1**: $C_{14}H_{11}NO_4$, M = 251.27, monoclinic, space group $C2/c$ (No. 15), a = 13.1691 (7), b = 8.3651 (5), c = 11.7215 (5) Å, V = 1208.38 (11) Å^3, T = 298 K, Z = 4, μ = 0.11 mm^{-1}, 2456 reflections measured, 1387 unique (R_{int} = 0.027), R_1 = 0.0582 (all data), wR_2 = 0.1305 (all data). Carbonyl groups assigned by C–O bond lengths. CCDC 173736. See http://www.rsc.org/suppdata/cc/b1/b110049a/ for crystallographic files in .cif or other format.

‡ *Crystal data* for **2**: $C_{14}H_{10}NO_5$, M = 258.23, monoclinic, space group $C2/c$ (no. 15), a = 13.5889 (5), b = 6.6994 (3), c = 13.5648 (6) Å, V = 1217.39 (9) Å^3, T = 298 K, Z = 4, μ = 0.11 mm^{-1}, 1972 reflections measured, 1057 unique (R_{int} = 0.031), R_1 = 0.0632 (all data)], wR_2 = 0.1455 (all data). Carbonyl groups assigned by C–O bond lengths. CCDC 173737.

§ Aniline (2.28 mL, 25 mmol), methyl-2-iodobenzoate (11.18 mL, 52.5 mmol), K_2CO_3 (7.26 g, 52.5 mmol), Cu (0.33 g, 5.2 mmol), and CuI (0.22, 1.2 mmol) combined in 20 mL di-*n*-butyl ether and refluxed under argon for 48 h. Column chromatography (4 : 1, hexane–ethyl acetate) followed by recrystallization from ethanol gave the coupled product in 81% yield. Base hydrolysis with NaOH in EtOH–H_2O (1 : 1) gave **3** in 99% conversion. Crystals were obtained from slow evaporation of an acetone–water solution of **3.**

¶ *Crystal data* for **3**: $C_{20}H_{15}NO_4$, M = 333.34, monoclinic, space group $P2_1/c$ (no. 14), a = 9.2755 (2), b = 10.7912 (4), c = 16.7186 (4) Å, V = 1658.61 (8) Å^3, T = 298 K, Z = 4, μ = 0.09 mm^{-1}, 5471 reflections measured, 2901 unique (R_{int} = 0.034), R_1 = 0.0539 (all data), wR_2 = 0.1138 (all data). Carbonyl groups assigned by C–O bond lengths. CCDC 173738.

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