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Single-Stranded Molecular Helical Assembly from a Self-Complementary Squaramide Compound

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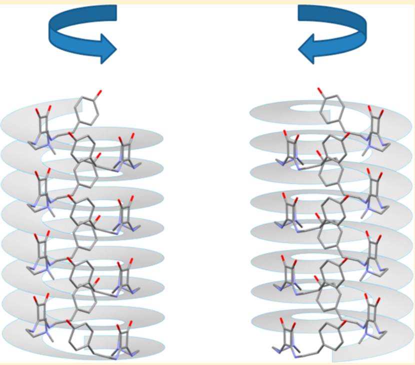
S *Supporting Information*

ABSTRACT: A new helical crystal structure of a disquaramide compound has been solved by means of direct methods from powder X-ray diffraction data. It contains a racemic mixture of alternating clock/anticlockwise rotating helices which are formed through an unprecedented combination of strong squaramide−squaramide and amine−phenol interactions, both in a head-to-tail fashion.



The helix is one of the most important structural motifs in nature due to its ubiquitous presence, from the molecular level to the astronomical scale.[1] Helicity shows relevant properties such as chirality and other geometric features which have attracted the attention of the scientific community.[2] Examples of helicity include the double-stranded DNA and the assembly of linear proteins into multistranded complexes which are responsible for the genetic information and diverse biological functions.[3] This fascinating natural motif has inspired the design and synthesis from unnatural backbones of a broad variety of artificial helices in the fields of supramolecular chemistry, asymmetric catalysis, biomimetics, etc.[4] Thus, the use of synthetic building blocks for the supramolecular assembling into helical polymers[5] has been successfully exploited in the past with metal-coordinated helical complexes[6] or self-assembled spiral nanoarchitectures from barbituric acid,[7] among many others.[8] In this sense, hydrogen-bonding is a key interaction due to its great directionality and strength which can be used to design highly stable and selective building blocks able to cooperatively drive the formation of polymeric assemblies.[9]

Disecondary squaramides form head-to-tail structures in the solid state thanks to the very strong self-complementary CO···HN intermolecular interaction which has been exploited recently by us to build self-assembling zwitterionic squaramides in the solid state.[10] With the objective of synthesizing hydrogen bonded assemblies with new topological features, we designed the nonsymmetrical squaramide compound **1** with both donor and acceptor terminal groups able to establish self-complementary hydrogen bonding interactions.

Assuming that the head-to-tail interaction can act as a template, in principle two types of interactions are possible: (a) cyclic and (b) polymeric, which could give rise to helical assemblies (Figure 1). In order to study this possibility, the asymmetric disquaramide **1** was synthesized through a two-step selective condensation of *N*,*N*-dimethylethylenediamine and tyramine with diethylsquarate in mild conditions (Figure 1a).[11]

Unfortunately, no crystals of 1 suitable for structure determination by single-crystal XRD could be obtained. Therefore, its crystal structure[12] was solved from laboratory X-ray powder diffraction data[13] by means of direct space methods using the computing program FOX.[14]

The experimental powder diffraction diagram was indexed with DICVOL04,[15] and the space group ($P2_1/c$) was deduced from the systematic absences. The presence of some impurities in the diffractogram hindered the indexing procedure. In accordance with the spectroscopic data (NMR-C, NMR-H) together with DSC and TGA curves, these impurities could be attributed to a squaramide ester generated in the first step of the synthesis (Figure 1). The cell and space group were validated with a Le Bail fit of the data using FullProf[16] (goodness of fit: $\mathrm{Chi}^2 = 2.83$, Rwp: 12.4). The used background (estimated from a set of experimentally read points and interpolated) and the resulting cell, zero error and shape parameters of the Le Bail fit were used in the structure solution procedure with FOX. The structure was solved using the parallel tempering algorithm implemented in FOX. The Z matrix was created with an optimized model by using SPARTAN,[17] and FOX was instructed to treat cyclobutene and phenol rings as rigid bodies. Three runs of two million

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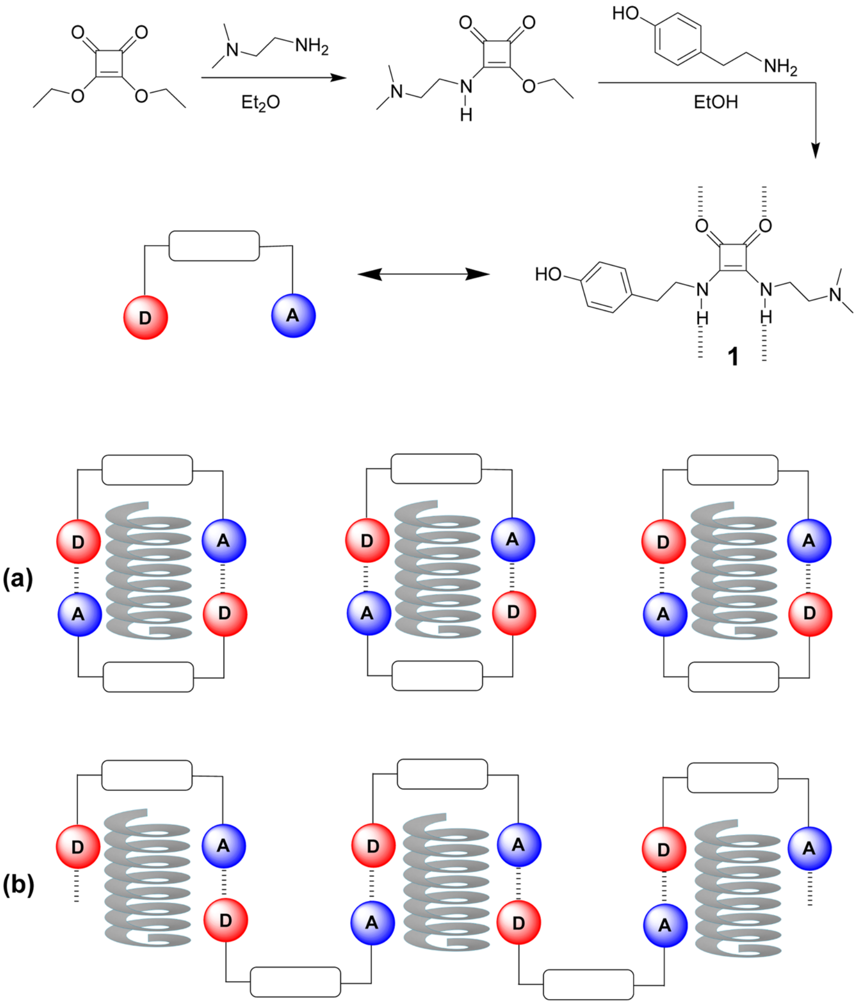

Figure 1. Synthesis of 1 and the different schematic self-assembling modes.

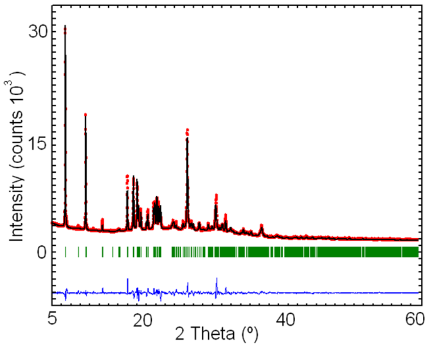

Figure 2. Results of final Rietveld refinements of **1**. Each plot shows the experimental powder XRD profile (red + marks), the calculated powder XRD profile (black solid line) and the difference profile (blue, lower line).

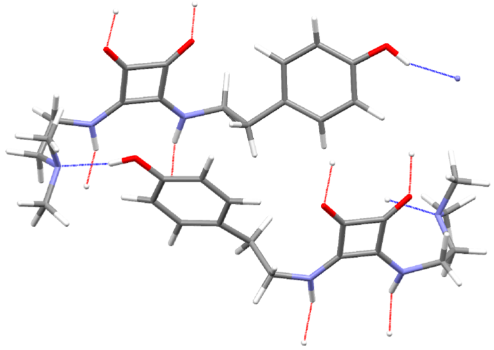

Figure 3. Intermolecular H-bonds in the helix building block.

trials each were performed and lead rapidly to a low overall cost function. The resulting structural models showed the same self-assembled synthon, and the best resulting crystal structure was the basis for subsequent Rietveld refinement[18] with Fullprof (see Figure 2).

X-ray crystallographic characterization revealed that **1** crystallizes in monoclinic system with space group $P2_1/c$ and one molecule in the asymmetric unit. As expected, the strong CO···HN self-complementary interaction[19] is established, giving place to a head-to-tail motif which acts as a skeletal template in the formation of peripheral amine−phenol interactions. The most remarkable feature of the structure is that discrete infinite helical assemblies are formed from this repetitive building block running in the direction of the squaramide dipole moment (Figure 3). The helices are formed in an antiparallel orientation, compensating the strong dipole moment of the squaramide ring in the crystal.

Helices are individually packed (following model *a* in Figure 1), connected to others through weak $CH\cdots\pi$ interactions between the methylamino group and the aromatic ring,[20] with

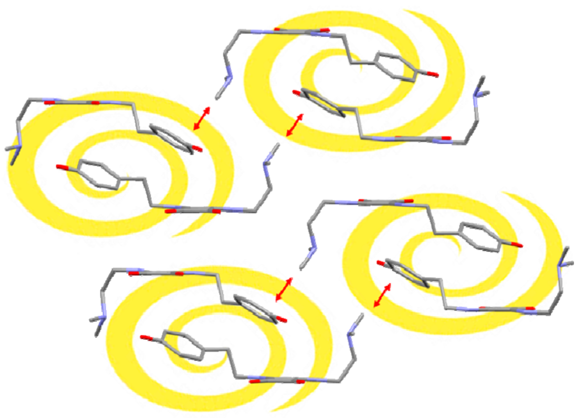

Figure 4. Helix-packing motifs via CH···π interactions.

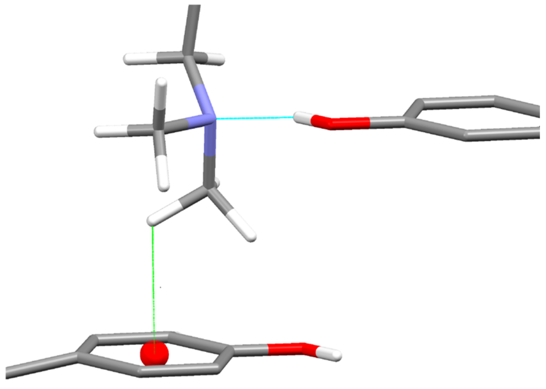

Figure 5. CH···π interaction between the methylamino group and the aromatic ring.

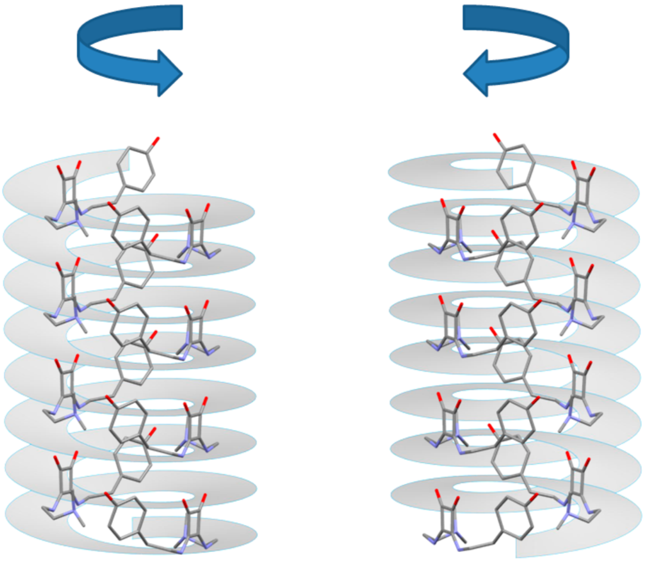

Figure 6. Clock and anticlockwise rotation of the two different helices in the racemic crystal.

centroid distance of 3.05 Å and C−H centroid angle of 109° (Figure 4).

This nitrogen atom is particularly electronegative due to the strong hydrogen bond with the phenol group which drives the methyl groups to interact efficiently with the face of the aromatic ring (Figure 5).

Although helical assemblies from an achiral compound as **1** can a priori form chiral crystals, a racemic mixture of alternating clock and anticlockwise spinning helices has been found (Figure 6) and no polymorphism has been observed so far.

In summary, we have studied via X-ray crystallography an unprecedented helix in a squaramide driven by a combination of two different head-to-tail interactions, which is remarkable in the field of crystal engineering and supramolecular chemistry. The good geometrical and donor/acceptor complementarity produces an optimal packing, which excludes the possibility of cavity formation. However, the introduction of more suitable substituents of the squaramide ring should permit the design of new helical hydrogen-bonded nanotubes based on the same strategy.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(12) Crystal data: $C_{16}H_{21}N_3O_3$. MW = 303.0. Unit cell dimensions: a = 10.2164(8) Å, b = 6.07487(12) Å, c = 25.9781(17) Å, β= 99.9674(16)°, V=1572.09(6) Å^3, Z = 4, d_{calc} = 1280 Mg/m^3 at room temperature. Rietveld refinement; 2θ range: 5.00−69.98; 5230 profile points; 94 refined variables; Rwp = 18.6%, Rp = 1.84% (compared to

the Le Bail fit: *R*wp = 11.00%, *R*p = 1.63%) (Figure 4). CCDC 953732 contains the crystallographic data.

(13) Laboratory X-ray powder diffraction data were collected at ambient temperature in a Panalytical X'Pert PRO MPD capillary configuration (0.7 milimeters of diameter capillary); focalizing elliptic mirror; Cu $K\alpha_{1+2}$, λ = 1.5418 Å; 0.01 radians Soller slits; PIXcel detector, active length 3.347°; 2θ range, 2°−70°, step size, 0.013°, data collection time, 60 h.

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