A Hydrogen-Bonded Supramolecular *meso*-Helix

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Keywords: Amides / Crystal engineering / Density functional calculations / Helical structures / Hydrogen bonds

A new one-dimensional hydrogen-bonded polymer with a unique *meso*-helical structure has been prepared from the spontaneous self-assembly in the solid-state of *meta*-substituted phenylene dioxamic acid diethyl ester monomers. The helical nature of this molecule and its self-complementary character, through intermolecular hydrogen bonding between oxamic acid ester functions, are the two main factors responsible for the crystalline aggregation process, as confirmed by both experimental X-ray crystallographic data and theoretical ab initio calculations.

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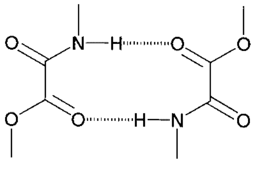
Self-assembly processes that lead to helical structures are common throughout biology and chemistry.[1,2] Protein α-helices and the DNA double helix are well-known biological examples which have inspired the work of synthetic chemists aiming to create chemical analogs of these complex structures.[3] A common feature of all these natural and nonnatural systems is the key role that noncovalent interactions play in determining the conformation and aggregation of the helical architecture. Hydrogen bonding, metal coordination bonding, solvophobic interactions, and electrostatic interactions are among the synthetic strategies to helical and multiple helical systems, both organic and inorganic (metalloorganic), prepared by means of molecular self-assembly.[4,5] Surprisingly, there is little known about *meso*-helical self-assembling systems within this very active field of helical structure research in supramolecular chemistry. The biopolymers α-amylose and cycloamylose, belonging to the class of carbohydrates, are interesting biological examples. Whilst the polysaccharide α-amylose consists of long linear chains having between one and two thousand glucose units with a right-handed helical structure, cycloamylose is a cyclic oligosaccharide of twenty six glucose units with a right- and a left-handed helix which are linked to give an overall cyclic *meso*-helical structure with two points of contraflexure.[6] To date, only three inorganic examples of *meso*-helical coordination polymers have been reported.[7] Here we present an organic example of such a system resulting from the solid-state aggregation of a dioxamic acid diester derivative, namely *N*,*N′*-1,3-phenylenebis(oxamic acid ethyl ester) (**1**). Single crystal X-ray analysis demonstrates the ability of this self-complementary molecule to assemble through double-hydrogen bond formation between the amide (proton donor) and carbonyl ester (proton acceptor) functions of oxamic acid ester groups (Scheme 1), which is a common motif in solid-state oxamide chemistry.[8] Preliminary density functional theory (DFT) calculations have been carried out on the simplest model system, *N*-phenyloxamic acid methyl ester (**2**), in order to support the experimental findings on the essential role of hydrogen bonding in determining the molecular conformation and molecular aggregation in the final structure.



Scheme 1. Schematic representation of the hydrogen-bonded oxamic acid ester dimer motif

Well-formed colorless prisms of **1** suitable for X-ray diffraction were obtained by crystallization from acetone of the initial material prepared as reported previously by ourselves and others.[9] The crystal structure reveals an infinite

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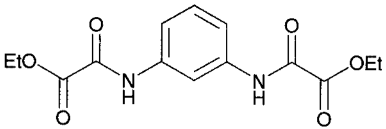
DOI: 10.1002/ejoc.200200544 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



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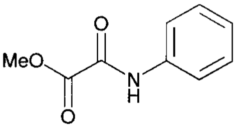

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chain array of molecules running along the c axis formed by repetition of the aforementioned centrosymmetric hydrogen-bonded oxamic acid ester dimeric unit (Figure 1). The rather long intermolecular hydrogen bond length [$d(\mathrm{H\cdots O}) = 2.30(4)$ Å] and the fairly linear intermolecular hydrogen bond angle [$\theta(\mathrm{N-H\cdots O}) = 158(3)°$] are within the category of weak to moderate hydrogen bonds.[10] The calculated dissociation energy for the hydrogen-bonded dimer of **2** is 20.0 kJ·mol^{-1}. This small, although non-negligible, hydrogen bond energy (E_{HB}) arises from the hydrogen-hydrogen and oxygen-oxygen repulsive contacts in addition to the attractive hydrogen-oxygen interactions in the resulting ten-membered hydrogen-bonded ring shown in Scheme 1, and defined in the graph-set notation as $R_2^2(10)$.

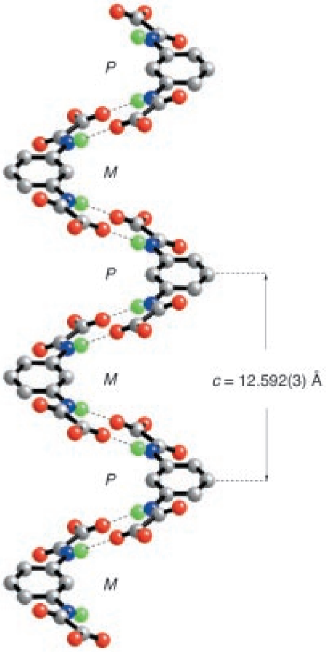

Figure 1. Ball-and-stick model representation of a single *meso*-helical chain of **1**; atoms are represented by spheres of arbitrary dimensions; carbon: gray, nitrogen: blue, oxygen: red, hydrogen: green; hydrogen bonds are drawn as dashed lines (ethyl groups and aromatic hydrogen atoms have been omitted for clarity)

Interestingly, the constituent molecules of twofold symmetry adopt a helical conformation, with the two oxalamide moieties tilted up and down, respectively, with respect to the plane of the *m*-phenylene spacer. The torsion angle around the N(amide)−C(phenylene) bond (φ) is as high as 32.6(5)°. This situation probably maximizes intermolecular hydrogen bonding along the chain while minimizing the intramolecular forced repulsive contacts between the amide hydrogen atom and its neighboring aromatic hydrogen atom. The energy calculations as a function of the torsion angle φ for **2** reveal that the minimum energy nonplanar conformation is more stable than the planar conformation by 18.6 kJ·mol^{-1}. The calculated φ value for the minimized conformer is 24.5°, in reasonable agreement with the experimental value found in the actual crystal structure. Indeed, a more constrained planar (not curved) molecule that self-assembles through this hydrogen-bonded oxamic acid ester motif would lead to a zigzag chain structure.[11] Because of the alternation of helical conformers of opposite chirality (M and P) around the inversion center, the resulting achiral chain adopts the rare *meso*-helical symmetry. Instead, typical enantiomeric (right- or left-handed) helices would be formed by aggregating helical molecules of the same chirality. Actually, the *meso*-helix can be described as resulting from helical reversal every half-turn of the helix. In this case, the helical character of the aggregating molecules gives rise to the growth of the helix, whereas the change in the twist sense of the helix is imparted by the centrosymmetric nature of the basic structure repeating unit shown in Scheme 1.

In the crystal lattice, there is a perfect alignment of helical conformers of the same chirality in the *meso*-helix as depicted in Figure 1. The spacing between benzene rings on neighboring homochiral molecules is 12.592(3) Å, which corresponds precisely to the lattice parameter c. The aromatic rings within each of the two columnar stacks are disposed in a parallel (nonfacial) arrangement and form an angle of 18.9(5)° with the axis of the *meso*-helix. Most importantly, there is an interesting packing of adjacent *meso*-helices related by simple translation in the b direction to give an infinite layer array of interdigitated (not intertwined) *meso*-helices in the bc plane (Figure 2).[12] This zipper-type intralayer packing involves multiple π-π stacking interactions between benzene rings on neighboring heterochiral molecules from two different *meso*-helices in the layer. Ultimately, this may also help to maintain the structural integrity of the *meso*-helical architecture. The aromatic rings are parallel displaced with a rather long centroid-centroid distance of about 6.6 Å.

On the other hand, the packing of adjacent layers in the a direction occurs via a screw axis according to the $C2/c$ space-group symmetry. This slipped interlayer packing results in a relatively short interplanar separation of 6.489(3) Å, which is equivalent to one half of the lattice parameter a (Figure 3). In this case, a sort of narrow pore is created along the c axis because of the presence of extensive polar interactions between amide carbonyl oxygen atoms and ester ethyloxy oxygen atoms of oxalamide groups on neighboring heterochiral molecules from two different *meso*-helices in adjacent layers. The shortest oxygen-oxygen contacts

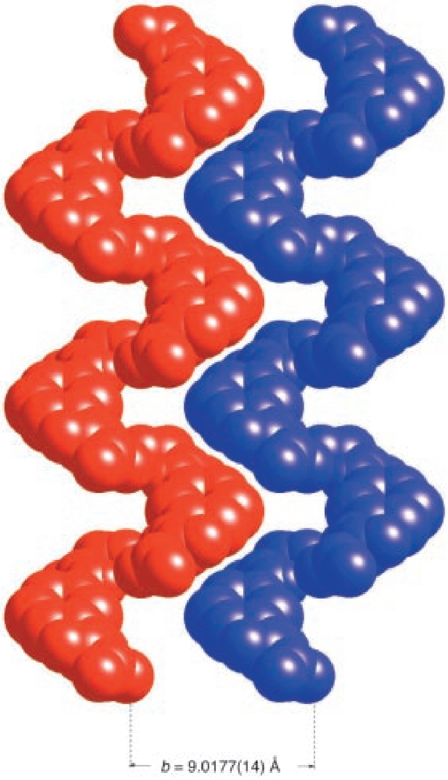

Figure 2. Space-filling model representation of two adjacent *meso*-helices of **1**;atoms from each *meso*-helix are represented by red and blue spheres of van der Waals radii (ethyl groups and aromatic hydrogen atoms have been omitted for clarity)

in the range 3.2−5.0 Å are, of course, larger than the sum of the van der Waals radii of the oxygen atom.

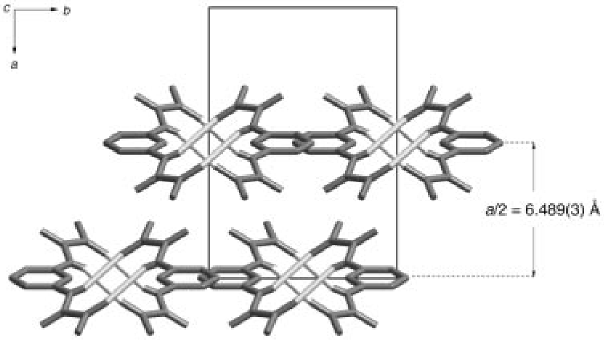

Figure 3. Stick model representation of the unit cell of **1**;covalent and hydrogen bonds are drawn as dark and light gray bars, respectively (ethyl groups and aromatic hydrogen atoms have been omitted for clarity)

In summary, the hydrogen-bonded achiral polymeric array of racemic monomer units of **1** constitutes an interesting example of a self-assembling supramolecular complex.[13] Thus, this unique *meso*-helical supermolecule fills a gap in the abundant literature on helical and multiple helical supermolecules prepared by means of molecular self-assembly, through either organic and/or inorganic approaches. Further developments emerge from this study concerning the potential of the oxamic acid ester functionality as a hydrogen-bonded supramolecular synthon in the field of crystal design and crystal engineering.[14] We are currently investigating the hydrogen bond-directed self-assembly of oligooxamic acid derivatives for the elaboration of novel ordered structures from molecules (molecular solids), which is a major goal of modern organic solid-state chemistry.

Experimental Section

X-ray Crystallographic Study of 1: Crystal data: $C_{14}H_{16}N_2O_6$, FW = 308.29, a = 12.977(3), b = 9.0177(14), c = 12.592(3) Å, α = 94.820(18)°, Z = 4, d = 1.395 g cm^{-3}, monoclinic, space group $C2/c$. Data collection: Enraf−Nonius CAD-4 diffractometer, Mo-K_α radiation, graphite monochromator, 293 K, 933 unique reflections, and 802 assumed as observed with $I > 2\sigma(I)$, μ = 0.110 mm^{-1}, Lorentz and polarization effects and absorption correction. Structural analysis and refinement: direct methods and full-matrix least-squares refinement on F^2 with SHELXS-97 and SHELXL-97.[15] Hydrogen atoms were not found but calculated (except for the amide hydrogen atom which was conveniently found), and refined with an overall isotropic thermal parameter. Refinement of 107 variables with anisotropic thermal parameters for all non-hydrogen atoms gave R = 0.0565 and R_w = 0.1604, with S = 0.827. Crystal drawings were carried out with the CRYSTAL MAKER program.[16] CCDC-175436 contains the supplementary crystallographic data for the structure reported in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk.

Computational Details: DFT calculations were performed on the monomer and dimer model systems of **2**, with structural dimensions taken from the crystal structure of **1**. In the energy calculations of the monomer model, only twisting around the N(amide)−C(phenyl) bond was considered by varying the torsion angle φ between 0 and 90°. The C_i symmetry constraint was considered in the energy calculations of the dimer model. All theoretical calculations were carried out with the hybrid B3LYP method, as implemented in the GAUSSIAN98 program, using the triple basis set proposed by Ahlrichs and co-workers.[17]

Acknowledgments

This work was supported by the Ministerio de Ciencia y Tecnología (Spain) through the Plan Nacional de Investigación Científica, Desarrollo e Innovación Tecnológica (I+D+I) (Projects ref. BQU2001-3017 and BQU2001-2928) and the Ramón y Cajal programs. We thank Profs. Miguel Julve and Francesc Lloret, and Dr. José A. Real for their continuing interest in this work and fruitful discussions during the preparation of the manuscript.

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Received October 2, 2002