The self-assembly and spontaneous resolution of a hydrogen-bonded helix

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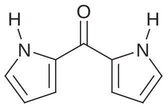
Although geometrically similar at the single-molecule level, the crystal structures of 2,2′-dipyrrolyl ketone and its synthetic precursor, 2,2′-dipyrrolyl thioketone, vary greatly at the supramolecular level: the ketone self-assembles *via* hydrogen bonding into supramolecular helices accompanied by a spontaneous resolution process to generate homochiral crystals, whereas the thioketone assembles into non-helical and racemic crystals composed of layers of alternating enantiomers held together by weak interactions.

The ability to encode molecules with well-defined non-covalent binding motifs, such as hydrogen bond sites, is critical in order to create predictable and useful solid-state supramolecular architectures of nanoscale dimensions.[1] During the synthesis of C_2-symmetric porphyrins, we prepared 2,2′-dipyrrolyl ketone **1** as previously described.[2] This simple molecule contains a high degree of encoded molecular recognition functionality. Of the twelve non-hydrogen atoms, three possess complementary hydrogen bond sites: two amine (N–H) donors and two carbonyl (C=O) lone pair acceptors. Additionally, the steric crowding of the C3 and C7 hydrogen atoms† on the two pyrrole rings forces the molecule into a twisted conformation. It was anticipated that the combination of these molecular features would translate into a helical supramolecular array held together by intermolecular N–H···O=C hydrogen bonds.[3]



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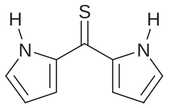

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We present here the crystal structures‡ of ketone **1** and its synthetic precursor, thioketone **2**. Single crystals of the ketone were obtained by layering a $CHCl_3$ solution of **1** with hexane. Ketone **1** self-assembles *via* hydrogen bonding into supramolecular helices, accompanied by a spontaneous resolution process to generate homochiral crystals. Interestingly, the sulfur analogue thioketone **2** crystallizes, under the same conditions, into a non-helical racemate.

Crystalline 2,2′-dipyrrolyl ketone **1** adopts a conformation in which both amine (N–H) groups point in the same direction as the ketone's carbonyl group [Fig. 1(*a*)]. Solution-state studies of the electric dipole moment of **1** attribute this conformational preference to the existence of intramolecular hydrogen bonding between the two N–H hydrogen atoms and the lone pair electrons of the carbonyl oxygen.[4] As expected, the crystal structure shows that the steric crowding of the C3 and C7 hydrogen atoms on the pyrrole rings does force the molecule to adopt a slightly twisted conformation. The result of these two effects is a convergent but non-coplanar self-complementary hydrogen bond surface. It is this spatial positioning of the molecular recognition sites that influences the self-assembly process in terms of the resulting supramolecular topology.

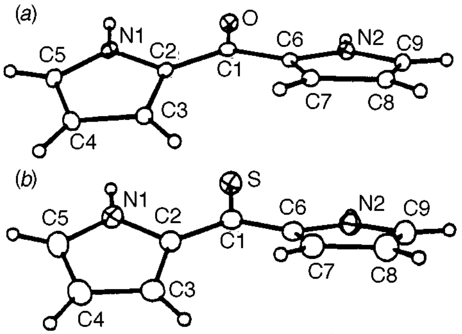

Fig. 1 Perspective view of (*a*) ketone **1** and (*b*) thioketone **2** showing the atom labeling schemes.

Ketone **1** crystal packs into supramolecular hydrogen bonded helices that extend indefinitely throughout the crystal lattice (Fig. 2). It is this extended network of strong N–H···O intermolecular hydrogen bonds (2.86 Å in length)§ that drives the formation of the helix between adjacent stacked columns of the ketone (Fig. 3). The dipyrrole building blocks are compressed within each of these columns so as to maximize favorable intermolecular π–π stacking interactions.¶ The path of the helix can easily be traced by following the hydrogen bonds counterclockwise around the two-fold screw axis of the helix (dashed lines in Fig. 3). Only one of the N–H groups is involved in intermolecular hydrogen bonding while the other N–H acts as a spectator. Two units of the ketone combine to make up a single turn of the helix generating a helical pitch of 5.9 Å.

At the molecular level, the crystal contains a single enantiomer of the ketone. This local chirality translates throughout the crystal into the formation of only left-handed (Λ)

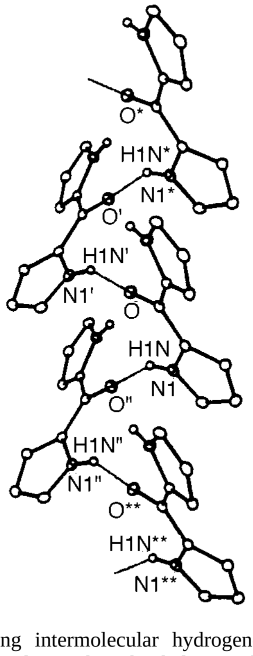

Fig. 2 View illustrating intermolecular hydrogen-bonded interactions between adjacent molecules within the helix. Carbon-bound hydrogen atoms have been omitted for clarity.

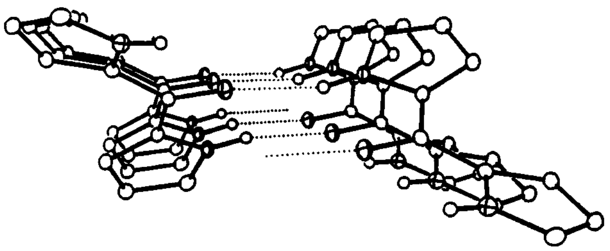

Fig. 3 Crystal packing diagram of ketone **1** viewed down the screw axis of an isolated helix. Intermolecular hydrogen bonds between stacked columns of molecular units are illustrated as dashed lines.

helices at the supramolecular level. There clearly must exist an auto-resolution process that is in effect during crystallization, whereby the pre-assembled helices *communicate* with the neighboring helices during the packing of the crystal lattice. Such chiral resolution processes are of interest because of their implications in the origin of homochirality.[5] Although only one crystal was sampled, we are assuming there exists an equal amount of crystals of both handedness in the bulk solid-state mixture.

At the molecular level, the geometry of thioketone **2** is virtually identical to that of the ketone. The only difference is a slightly increased interplanar angle (31.9°) presumably due to the larger sulfur atom, which forces the N–H groups slightly further out of coplanarity [Fig. 1(*b*)]. A significant difference is seen, however, at the supramolecular level, where a non-helical racemic crystal is generated falling into the achiral space group *Pbca*. The thioketone packs into antiparallel layers of opposing enantiomers. These layers appear to be held together by very weak interactions between the amine hydrogen and the sulfur atom of adjacent but offset enantiomers (dashed lines in Fig. 4) about which an inversion center is created. It is not clear whether these interactions can be rigidly defined as hydrogen bonds as the NH···S distance is close to the sum of the van der Waal's radii of these atoms.‖ It is clear that the replacement of the strong hydrogen bond acceptor (the carbonyl oxygen atom) with a weaker acceptor (the sulfur atom)[6] has a great effect on the supramolecular architecture. We attribute this to the change in the driving force for crystal packing from strong hydrogen bonds in the case of ketone **1** to weaker van der Waal's interactions in the case of thioketone **2**.

We have shown here that although the geometries of both ketone **1** and thioketone **2** are virtually identical at the molecular level, they vary greatly in their supramolecular topologies.[7] Where ketone **1** packs primarily *via* strong hydrogen-bonding interactions into helical arrays, the crystal packing of the thioketone **2** seems to be driven mainly by weaker interactions. The hydrogen-bonded network of ketone **1** results in a helical architecture that may play a role in the resulting auto-resolution. The effects of varying recrystallization conditions such as solvent, temperature and the presence of seed crystals are currently being investigated. This body of work demonstrates how the appropriate tailoring of prefabricated molecular components can lead to interesting supramolecular structures. Great care must be taken when choosing the molecular recognition constituents as the solid-state architecture is clearly governed by their attributes.

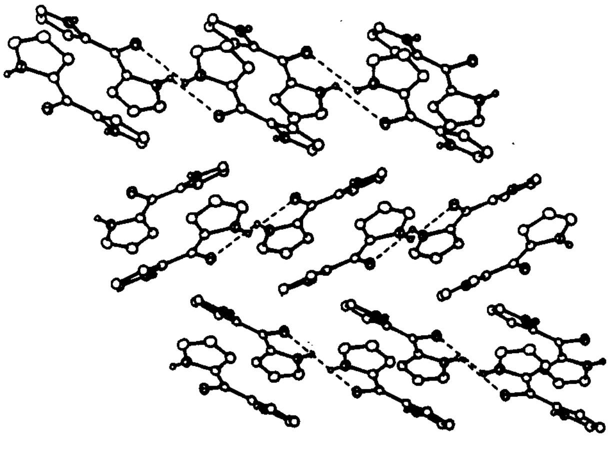

Fig. 4 Cross-section of the crystal packing diagram of thioketone **2** illustrating the herringbone arrangement of stacked antiparallel layers. Carbon-bound hydrogen atoms have been omitted for clarity. Dashed lines represent weak N–H···S contacts between offset enantiomers.

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Notes and references

† The numbers refer to the atom labelling scheme in Fig. 1(*a*).

‡ *Crystal data* for **1**: $C_9H_8N_2O$, M = 160.17, orthorhombic, space group $P_12_12_12_1$, (No. 19), a = 5.919 (1), b = 8.569 (1), c = 14.959 (1) Å, V = 758.7 (2) Å^3, T = −100 °C, Z = 4, μ = 0.095 mm^{-1}, number of reflections and independent reflections = 4159, $R_1(F)$ = 0.0594 [$F^2 \geq 2\sigma(F^2)$], wR_2 (F^2) = 0.1249 (all data). The absolute configuration of **1** was determined by refinement of the Flack parameter. For **2**: $C_9H_8N_2S$, M = 176.23, orthorhombic, space group *Pbca* (No. 61), a = 7.2510 (2), b = 13.8734(4), c = 16.4273 (4) *Å*, V = 1675.31 (8) Å^3, T = −60 °C, Z = 8, μ = 2.927 mm^{-1}, number of reflections = 2169, number of independent reflections = 1113, $R_1(F)$ = 0.0391 [$F^2 \geq 2\sigma(F^2)$], wR_2 (F) = 0.1019 (all data). In both cases, the amine hydrogen atoms were placed in calculated positions. CCDC 182/1178. Crystallographic data in CIF format are available from the RSC web site, see: http://www.rsc.org/suppdata/cc/1999/719/

¶ The shortest distance between stacked π-systems is 3.45 Å in the crystal. The aromatic pyrrole rings appear to be arranged so as to maximize offset π–π stacking.

§ The hydrogen bond length refers to the center-to-center distance between the carbonyl oxygen and N–H nitrogen obtained directly from the crystal structure.

‖ The N···S distance between antiparallel dimers is 3.50 Å which is close to the sum of the van der Waals' radii of sulfur and nitrogen (3.4 Å).

1 D. S. Lawrence, T. Jiang and M. Levett, *Chem. Rev.*, 1995, **95**, 2229; J.-M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, Germany, 1995.

2 J. A. de Groot, J. H. Koek and J. Lugtenburg, *Recl. Trav. Chim. Pays-Bas*, 1981, **100**, 405.

3 For examples of supramolecular helices, see: S. Hanessian, M. Simard and S. Roelens, *J. Am. Chem. Soc.*, 1995, **117**, 7630; T. Gulik-Krzywicki, C. Fouquey and J.-M. Lehn, *Proc. Natl. Acad. Sci. U.S.A.*, 1993, **90**, 163; S. Geib, C. Vincent, E. Fan and A. D. Hamilton, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 119; S. Sun, J. F. Britten, C. N. Cow, C. F. Matta and P. H. M. Harrison, *Can. J. Chem.*, 1998, **76**, 301; A. E. Rowan and R. J. M. Nolte, *Angew. Chem., Int. Ed.*, 1998, **37**, 63.

4 H. Lumbroso, C. Liegeois, G. C. Pappalardo and C. G. Andrieu, *J. Mol. Struct.*, 1984, **112**, 85; for an example of the solid state structure of a monopyrrolyl ketone, see: W. S. Sheldrick and W. Becker, *Acta Crystallogr., Sect. B*, 1978, **34**, 2929.

5 M. Suárez, N. Branda, J.-M. Lehn, A. Decian and J. Fischer, *Helv. Chim. Acta*, 1998, **81**,1; for a general discussion of non-chiral molecules packing into chiral crystals, see: J. Jacques, A. Collet and S. H. Wilen, *Enantiomers, Racemates and Resolution*, Wiley Interscience, New York, 1981; for other examples of hydrogen bond directed resolution in the solid state, see: H. Koshima, E. Hayashi, T. Matsuura, K. Tanaka, F. Toda, M. Kato and M. Kiguchi, *Tetrahedron Lett.*, 1997, **38**, 5009; L. Leiserowitz and M. Weinstein, *Acta Crystallogr., Sect. B*, 1975, **31**, 1463 and references cited therein.

6 V. R. Pedireddi, S. Chatterjee, A. Ranganathan and C. N. R. Rao, *J. Am. Chem. Soc.*, 1997, **119**, 10867; C. E. Bugg and U. Thewalt, *J. Am. Chem. Soc.*, 1970, **92**, 7441.

7 For a similar comparison of urea and thiourea, see: D. Mullen, *Acta Crystallogr., Sect. B*, 1982, **38**, 2620 and refs. therein.

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