

Crystal Engineering of a Liquid Crystalline Piperazinedione†,‡

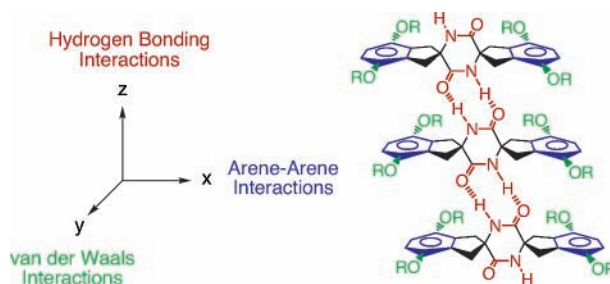
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ABSTRACT



A molecule designed to self-assemble via hydrogen bonding, arene-arene, and van der Waals interactions and expected to possess thermotropic liquid crystalline properties has been synthesized and characterized. Results support the validity of an assembly paradigm based on incorporation of chemically orthogonal and spatially independent recognition elements in the molecular building blocks.

Understanding and harnessing noncovalent interactions is of universal importance to biology, chemistry, and materials science.¹ We postulated that crystal packing might be controlled by incorporation of three chemically orthogonal molecular recognition elements that are also spatially independent of each other and designed a family of piperazinedione-containing molecules to test this hypothesis (Figure 1).² The central piperazine-2,5-dione ring should favor formation of supramolecular one-dimensional tapes through reciprocal amide-to-amide hydrogen bonding.³ Control of second and third dimensional order depends on arene-to-

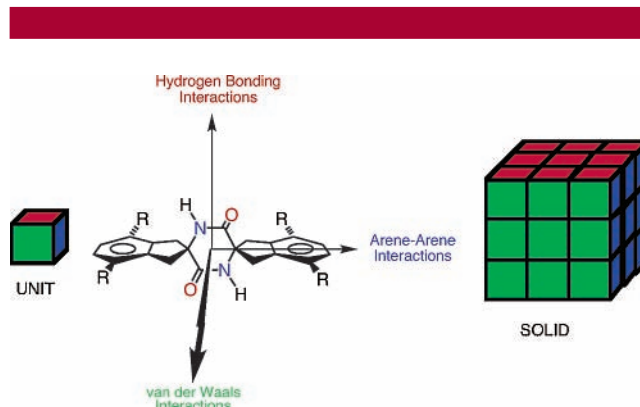


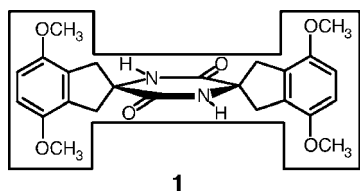
Figure 1. Assembly paradigm: molecular units incorporating three geometrically and chemically independent recognition elements might assemble predictably into a solid.

arene interactions and van der Waals contacts. Arene interactions have been recognized as important, from the packing of small molecules to the stabilization of protein tertiary structures.⁴ van der Waals attractive interactions contribute significantly to crystal lattice organization as is evidenced by the tendency of organic compounds to achieve closest packing in the solid state.^{1,5}

† Dedicated to Professor E. J. Corey on the occasion of his 75th birthday.

‡ Organic Crystal Engineering with Piperazine-2,5-diones. Part 5.

(1) (a) Kitaigorodsky, A. I. *Molecular Crystals and Molecules*; Academic Press: New York, 1973. (b) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, 1989. (c) Wright, J. D. *Molecular Crystals*, 2nd ed.; Cambridge University Press: Cambridge, 1995. (d) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, Germany, 1995. (e) *The Crystal as a Supramolecular Entity*; Desiraju, G. R., Ed.; John Wiley & Sons, Ltd.: Chichester, England, 1996. (f) *Crystal Engineering: The Design and Application of Functional Solids*; Seddon, K. R.; Zaworotko, M., Eds; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1999. (g) *Organised Molecular Assemblies in the Solid State*; Whitesell, J. K., Ed.; John Wiley & Sons, Ltd.: Chichester, England, 1999. (h) Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*; Oxford University Press: Oxford, 1999. (i) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; John Wiley & Sons, Ltd.: Chichester, England, 2000, and references cited therein.



We have previously observed that the crystal packing of compound **1** follows the assembly paradigm given in Figure 1. Hydrogen-bonded tapes (Figure 2, one tape is shown in

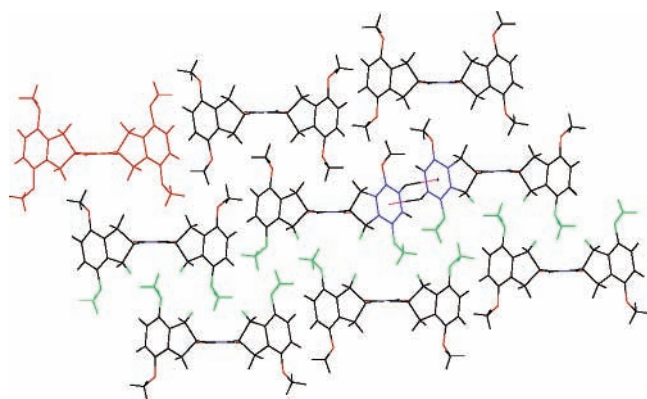


Figure 2. Cross section perpendicular to the hydrogen bonding axis from the crystal structure of compound **1**. Molecular recognition elements include hydrogen-bonded tapes (red), arene edge-to-face interactions (blue), and van der Waals contacts (green).

red) associate via arene edge-to-face interactions (blue) to give sheets that maximize van der Waals contacts (green) in the solid.^{2a} Other piperazinediones with topology similar to **1** pack similarly.^{2b}

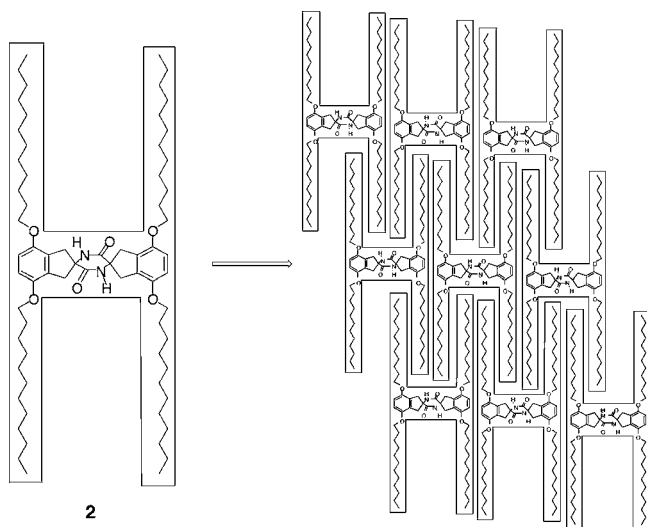


Figure 3. Hypothetical tape cross section and anticipated crystal packing viewed perpendicular to the hydrogen bonding axis for compound **2**.

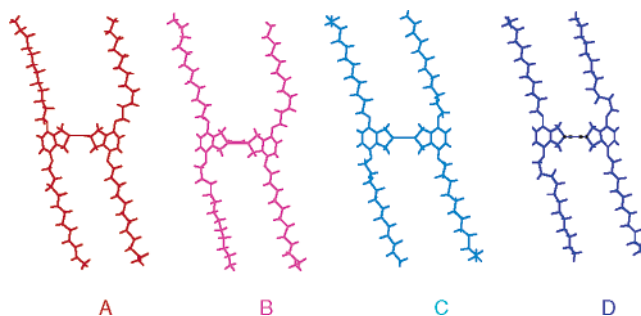


Figure 4. Conformers present in the crystal structure of **2**.

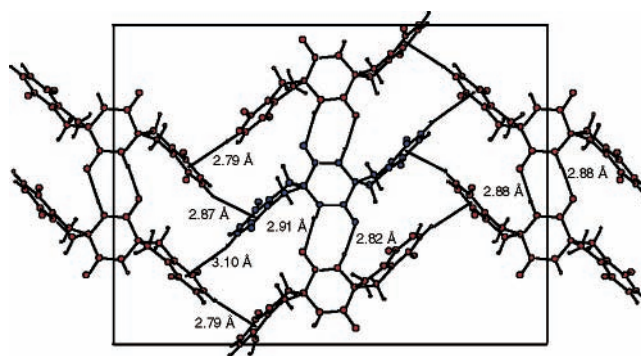


Figure 5. View of the unit cell (shown) from the crystal structure of **2** illustrating hydrogen bonding and arene edge-to-face interactions between conformers A (red) and D (dark blue). Conformers B and C, which coexist with A and D, and the dodecyl chains of conformers A and D have been omitted for clarity.

Poly(methylene) chains longer than butyl generally adopt an extended zigzag conformation and pack in either a parallel or an antiparallel fashion in the crystalline state.⁶ Given this fact and the observed packing in the crystal of **1**, we

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(3) Many examples of “ladder-like” tapes have been reported. See: MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383–2420.

(4) (a) Waters, M. L. *Curr. Opin. Chem. Biol.* **2002**, *6*, 736–741. (b) Hobza, P.; Selzle, H. L.; Schlag, E. W. *J. Am. Chem. Soc.* **1994**, *116*, 3500–3506. (c) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768–4774. (d) Burley, S. K.; Petsco, G. A. *J. Am. Chem. Soc.* **1986**, *108*, 7995–8001. (e) Karlström, G.; Linse, P.; Wallqvist, A.; Jönsson, B. *J. Am. Chem. Soc.* **1983**, *105*, 3777–3782. (f) Ribas, J.; Cubero, E.; Luque, F. J.; Orozco, M. *J. Org. Chem.* **2002**, *67*, 7057–7065. (g) Nakamura, K.; Houk, K. N. *Org. Lett.* **1999**, *1*, 2049–2051. (h) Kim, E.; Paliwal, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1998**, *120*, 11192–11193. (i) Umezawa, Y.; Tsuboyama, S.; Honda, K.; Uzawa, J.; Nishio, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1207–1213. (j) Paliwal, S.; Geib, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1994**, *116*, 4497–4499.

(5) (a) Depero, L. E. *Adv. Mol. Struct. Res.* **1995**, *1*, 303–337. (b) Perlestein, J. *NATO Sci. Ser. C* **1999**, *538*, 23–42. (c) Desiraju, G. R. *Nature Mater.* **2002**, *1*, 77–79. (d) Organic zeolites are exceptions; see: Feldman, K. S.; Liu, Y.; Saunders, J. C.; Masters, K. M.; Campbell, R. F. *Heterocycles* **2001**, *55*, 1527–1554 and references therein.

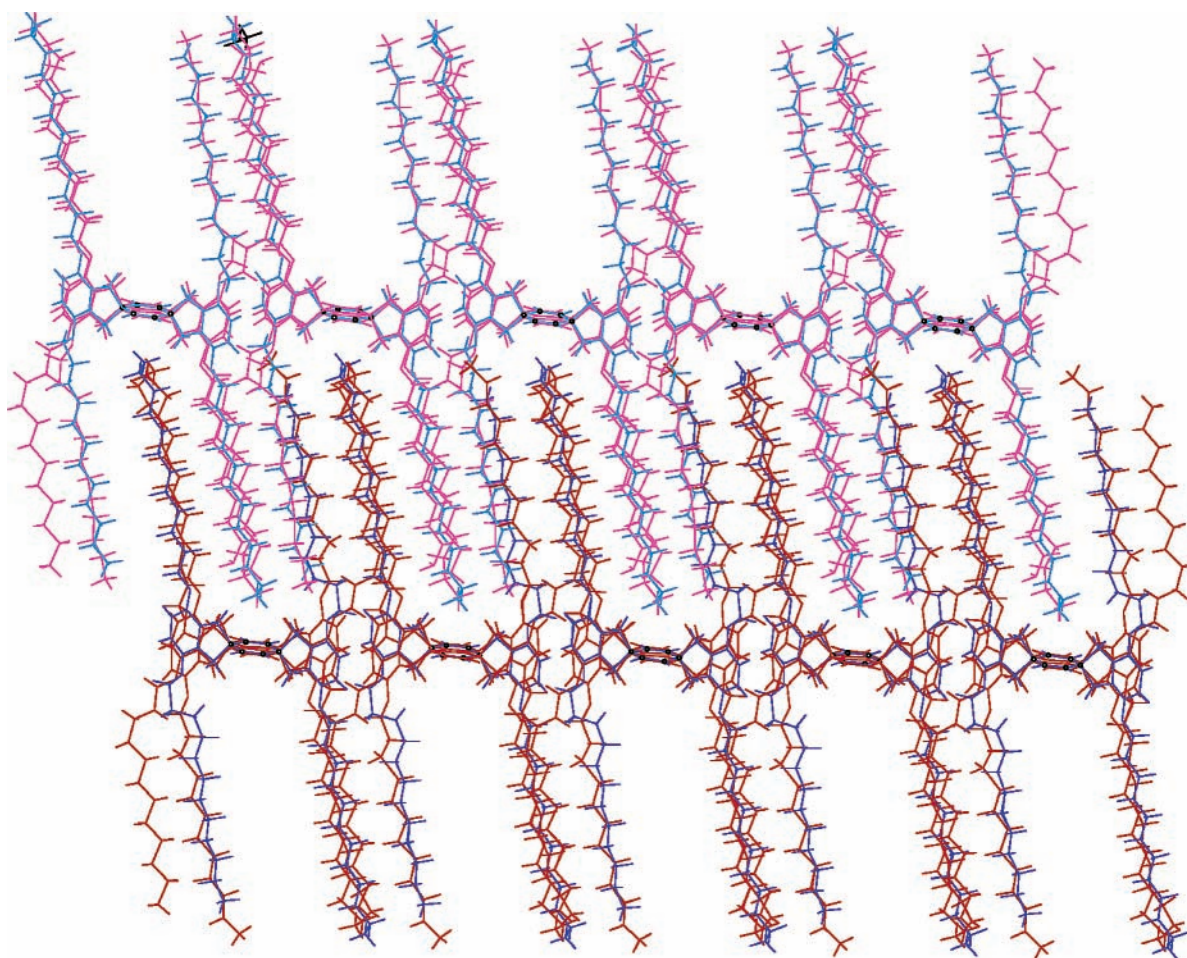


Figure 6. View of sheet interdigitation from the crystal structure of **2** looking down the hydrogen-bonded tape axis. For clarity, only conformers B (pink) and C (light blue) are shown in the top sheet and only conformers A (red) and D (dark blue) are shown in the bottom sheet.

postulated that tapes with elongated cross sections would pack via reciprocal hydrogen bonding, arene edge-to-face interactions, and van der Waals-driven interdigitation of the alkyl tails in extended conformations (Figure 3). Such molecules should exhibit liquid crystalline properties.

Compound **2** was prepared as depicted in Scheme 1. Experimental details for the synthesis of **2** are given in Supporting Information.

Microcrystals of **2** were grown at room temperature by evaporation of a 2-propanol solution and the structure determined by X-ray diffraction at 100 K at the Advanced Photon Source at Argonne National Laboratory.⁷

Four conformers were present in the crystal of **2** (Figure 4). Conformers A and B are similar and coreside at a general position in the unit cell, while conformers C and D are similar and coreside at a position with inversion of symmetry. Despite the greater conformational complexity, *the crystal packing of 2 follows the anticipated assembly paradigm*: piperazinediones engage in reciprocal hydrogen bonding to form tapes (Figure 5), lateral neighbor tapes associate via arene edge-to-face interactions to form sheets (Figure 5), and

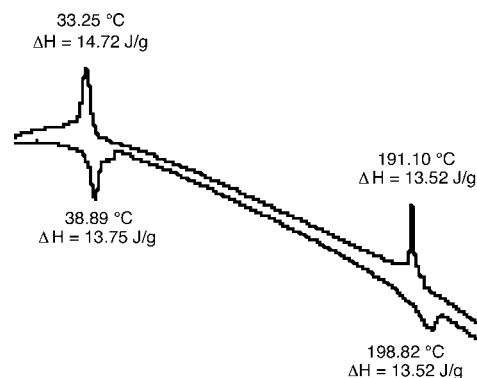
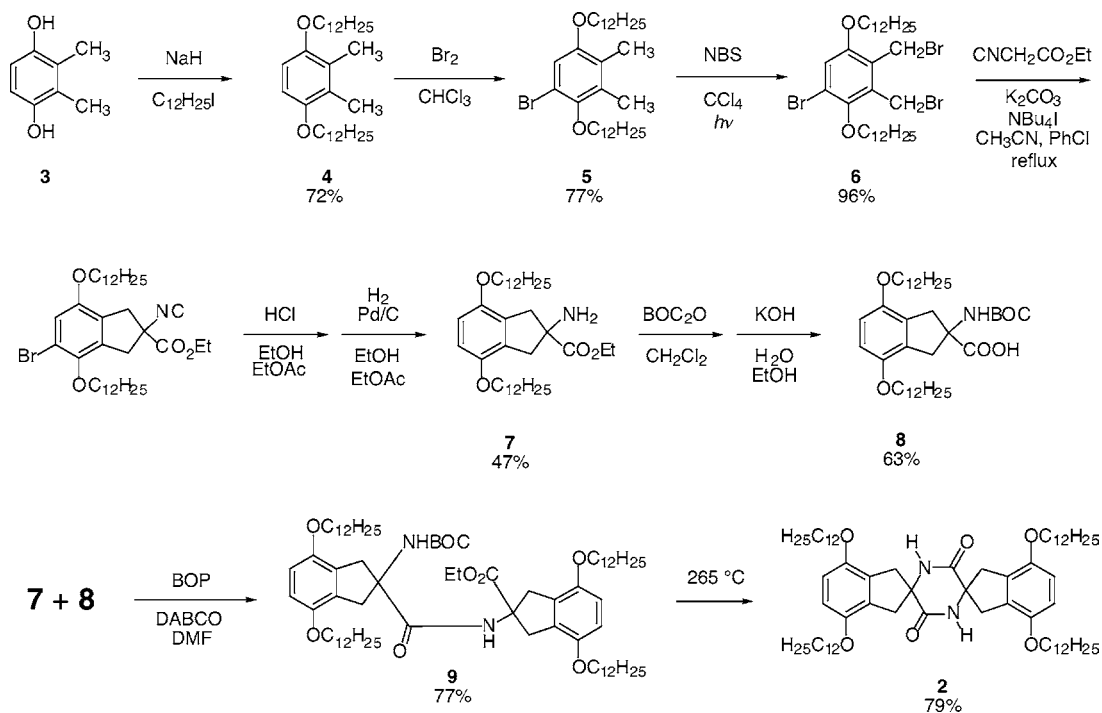


Figure 7. Modulated DSC curve for compound **2**. Heating and cooling rate was 5 °C/min.

sheets nest to maximize van der Waals contacts in the solid (Figure 6).

The melting behavior of **2** was examined by modulated differential scanning calorimetry (Figure 7). Reversible phase

Scheme 1. Synthesis of Piperazinedione **2**



transitions were noted near 35 °C (solid to liquid crystal) and 195 °C (liquid crystal to isotropic). These transitions were also observed by optical microscopy under cross-polarized light.

Solid-state structure and bulk properties are inextricably linked. Design of compounds that exhibit expected properties from a predictable crystal packing is a primary goal of crystal engineering. The assembly paradigm given in Figure 1 was employed in the design of **2**. The validity of this paradigm is supported by experimental results with **2**.

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Supporting Information Available: Synthetic procedures for the preparation of **2**, X-ray crystallographic information file (CIF) for **2**, PDF files for Figures 2 and 6, and photographs depicting the temperature-dependent birefringence of **2**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(6) For example, the hydrocarbon tails of stearic acid pack in a parallel fashion, producing a sheet structure that resembles a lipid bilayer. Adjacent sheets associate by carboxylic acid dimer formation. See: Kaneko, F.; Sakashita, H.; Kobayashi, M.; Kitagawa, Y.; Matsuura, Y.; Suzuki, M. *Acta Crystallogr., Sect. C* **1994**, *50*, 247–250.

(7) Crystal data for **2**: C₆₈H₁₁₄N₂O₆; *M* = 1055.61 g/mol, monoclinic, *P*2₁/*c*, colorless prism measuring 0.02 × 0.03 × 0.07 mm, *T* = 100(2) K, *a* = 21.981(4), *b* = 18.298(4), *c* = 24.801(5) Å, β = 108.72(3)°, *V* = 9447(3) Å³, *Z* = 6, *D*_c = 1.113 Mg/m, μ = 0.069 mm⁻¹, *T*_{max} = 1.0000, *T*_{min} = 0.5915, GOF on *F*² = 1.098, *R*₁ = 0.1160, *wR*₂ = 0.2971 for all 25086 independent observed reflections.