



Self-assembly of enantiopure 2,2'-dimethylbiphenyl-6,6'-dicarboxylic acid. Formation of chiral squares and their columnar stacking

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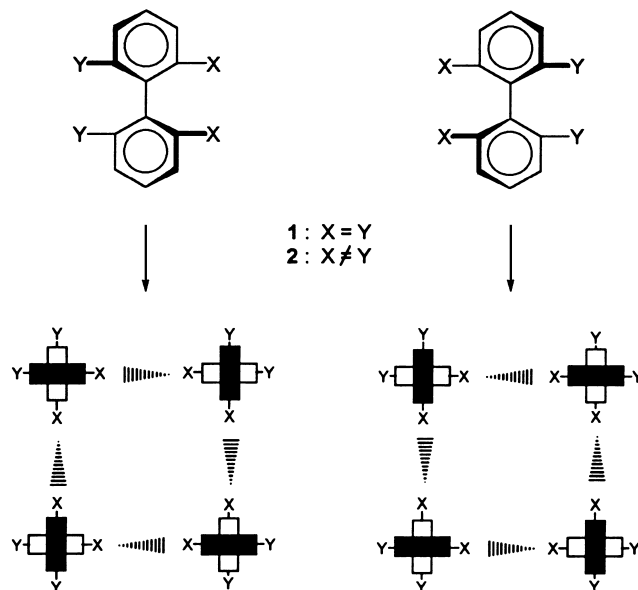
Abstract

The title (*R*)-diacid has been found to self-assemble as hydrogen-bonded cyclotetramers in solution as well as in the solid phase; in the crystal the tetramers are stacked into chiral columns. In contrast, the racemic diacid forms infinite zig-zag chains of molecules of alternating chirality. © 1999 Published by Elsevier Science Ltd. All rights reserved.

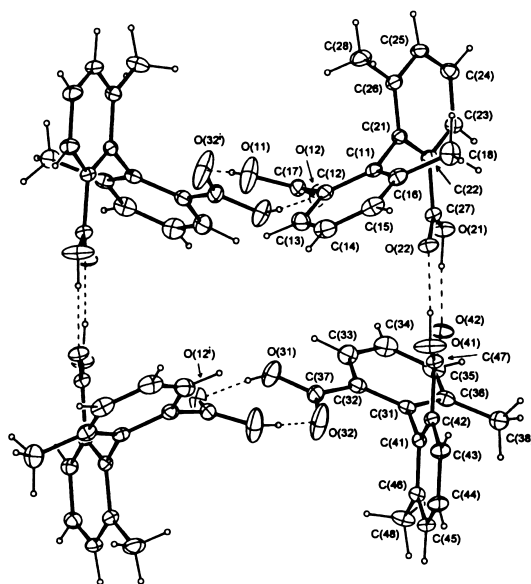
The fascinating architecture of achiral zeolites^{1,2} inspires the design of chiral microporous frameworks employing supramolecular self-assembly³ as the synthetic tool. Our recent discovery that biphenyl-2,2',6,6'-tetracarboxylic acid **1a** (**1a**; X=Y=COOH) self-assembles, in crystal, under formation of a two-dimensional network set up from cyclotetrameric hydrogen-bonded square compartments⁴ opens interesting vistas in this direction. The stereochemistry of the supramolecular squares attracts particular attention. In contrast to the individual molecules of the tetraacid **1a**, which possess D_{2d} symmetry and are thus achiral, the self-assembled cyclotetramers possess D_4 symmetry (Fig. 1) and are chiral. Squares of opposite chirality alternate⁴, however, in the infinite grid which is accordingly achiral.

Homochirality of the supramolecular network can be obtained if the individual self-assembling molecules (tectons) are chiral and enantiomerically pure. The requisite stereochemical transformation of the achiral tecton **1** (X=Y) can be attained by a pairwise differentiation of the *ortho* substituents giving rise to chiral molecules **2** (X≠Y; C_2 symmetry). If both substituents X and Y in **2** are endowed with hydrogen-bonding ability, infinite homochiral square networks can result.⁵ If only one substituent (X) is capable of hydrogen bonding, discrete homochiral squares of D_4 symmetry should be produced. We have chosen the (*R*)-isomer of the title diacid **2a** (**2a**; X=COOH; Y=CH₃) as a simple model for self-assembly into the discrete chiral cyclotetramers.

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Figure 1. Formation of tetramers from **1** and **2**

Single crystal X-ray diffraction of the enantiopure⁶ diacid (*R*)-**2a** shows⁷ that there are two crystallographically independent molecules participating in the cyclotetramer formation (Fig. 2). The two molecules (A and B) differ slightly in their conformation, the dihedral angles subtended by the mean aromatic planes being $82.70(7)^\circ$ in A and $80.82(8)^\circ$ in B. More marked differences appear in the orientation of the carboxyl groups: the aromatic vs. COO dihedral angle⁸ being $42.1(2)^\circ$ [C(17)] and $26.2(1)^\circ$ [C(27)] for molecule A but $5.8(4)^\circ$ [C(37)] and $21.9(1)^\circ$ [C(47)] for molecule B. As a consequence, the resulting cyclotetramer is distorted from the ideal arrangement. Taking into account the van der Waals radii, the space inside the distorted cyclotetramer is approximately $6.8 \times 1.8 \text{ \AA}$.

Figure 2. View of the tetramer of (*R*)-**2a** (ORTEP, 30% probability ellipsoids). Hydrogen bonds are drawn as dotted lines

As can be seen in Fig. 3, the cyclotetramers are stacked in an eclipsed manner along the crystallographic *b*-axis resulting in chiral columns generated by translation. The distance between the tetramers in this direction is 9.012 Å ($=b$) which excludes any possibility of a π -interaction of the phenyl groups. The stacks are arranged in a parallel manner in the remaining two directions (Fig. 4A). The chiral square and column-forming ability is a consequence of the enantiopure diacid **2a**. Heterochiral alignment is preferred by the racemic diacid. In the crystal of the racemate,^{9–11} the molecules of alternating chirality are linked by double hydrogen bonds into zig-zag chains (Fig. 4B).

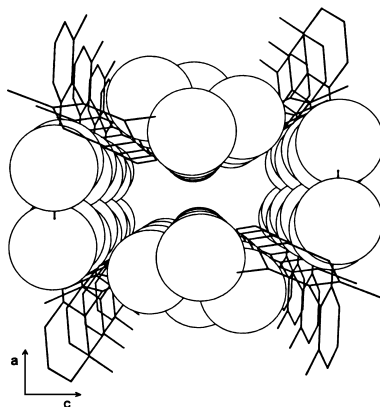


Figure 3. Perspective view of the column of (*R*)-**2a** tetramers down the *b*-axis. Oxygen atoms are drawn as circles of van der Waals diameter

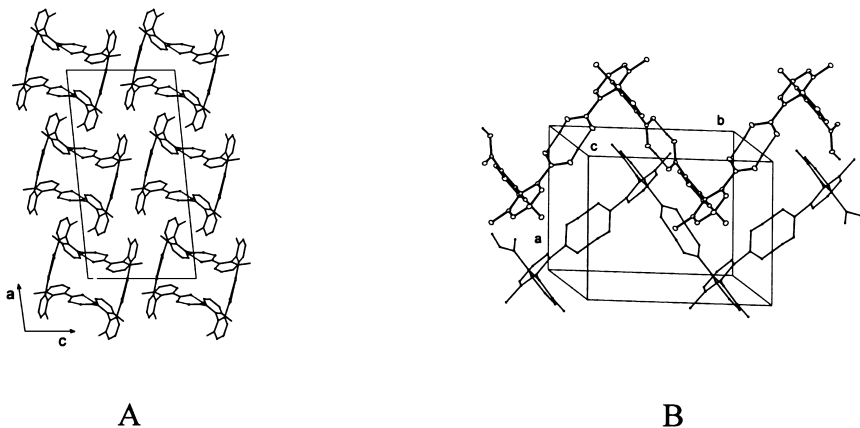


Figure 4. Comparison of crystal packing of (*R*)-**2a** (cyclotetramers, A) and (*RS*)-**2a** (zig-zag chains, B)

Notably, the fundamental difference in self-assembly of the homochiral and racemic diacid **2a** pervades in low polar solvents. Vapour pressure osmometry of the homochiral diacid (*R*)-**2a** indicates an apparent degree of association of ~ 4 in CHCl_3 solution¹² indicating formation of the discrete cyclotetrameric species. In contrast, polymeric chains (evidenced by the X-ray studies) prevail with the insoluble racemic form (*RS*)-**2a** under comparable conditions.

To our best knowledge, the above results represent the first experimental demonstration of the fundamental difference in the self-assembly of an enantiopure biaryl diacid and its racemate, suggesting at the same time a new access to the design of chiral microporous structures. The simplicity of the biaryl will facilitate a structure tuning study directed to expansion of the effective diameter of the chiral cavities inside the self-assembled squares and columns (channels).

Acknowledgements

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6. Absolute configuration of the diacid **2a** has been determined previously by chemical correlation: McGinn, F. A.; Lazarus, A. K.; Siegel, M.; Ricci, J. E.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 476.
7. Crystal data for C₁₆H₁₄O₄ (*R*)-**2a**: *M*=270.27, mp 216°C, grown from heptane–ether by slow evaporation; [α]_D²⁰ –21.3 (*c* 1, MeOH) (reported in: Siegel, M.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 473); mp 207–211°C, [α]_D²³ –22 (*c* 1, MeOH) (reported in: Kanoh, S.; Muramoto, H.; Kobayashi, N.; Motoi, M.; Suda, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3659); mp 213–214°C, [α]_D²⁵ –21.3 (*c* 1, MeOH), monoclinic, *a*=24.964(3), *b*=9.012(1), *c*=12.990(2) Å, β =96.32(1)°, *U*=2904.7(7) Å³, *T*=150 K, space group *C2* (no. 5), *Z*=8, μ (Mo-*K*)=0.089 mm⁻¹, 3764 reflections measured, 3040 unique (*R*_{int}=0.021), 2800 observed [*I*>2 σ (*I*)] used in calculations (SIR [Cascarano, G. *Acta Crystallogr.* **1996**, *A52*, C-79], SHELXL93 [Sheldrick, G. M. *SHELXL-93. Program for Crystal Structure Refinement from Diffraction Data*; University of Göttingen, 1993]). The final *R*(*F*²) was 0.032 for observed data. The atomic coordinates, bond lengths and angles were deposited by CSD and can also be obtained in the form of the CIF file from the author (J.P.) by e-mail: podlaha@natur.cuni.cz.
8. Notably, a comparable tilt of the carboxyl group can be found in the crystal of the enantiopure as well as the racemic (vide infra) diacid **2a**, suggesting that it is not related to a particular supramolecular architecture. Conceivably, the tilt stabilizes the intermolecular hydrogen bonds since the acid strength of aromatic carboxylic acids is a function of the out-of-plane angle.
9. Crystal data for C₁₆H₁₄O₄ (*RS*)-**2a**: *M*=270.27, mp 241–243°C (heptane–ether) (reported in: Kanoh, S.; Muramoto, H.; Kobayashi, N.; Motoi, M.; Suda, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3659); mp 240–241°C, monoclinic, *a*=9.009(1), *b*=11.274(4), *c*=14.363(3) Å, β =107.34(1)°, *U*=1392.5(6) Å³, *T*=150 K, space group *P2*₁/*n* (non-standard setting of *P2*₁/*c*, no. 14), *Z*=4, μ (Mo-*K*)=0.093 mm⁻¹, 2606 reflections measured, 2446 unique (*R*_{int}=0.016), 2124 observed [*I*>2 σ (*I*)] used in calculations (SIR [Cascarano, G. *Acta Crystallogr.* **1996**, *A52*, C-79], SHELXL93 [Sheldrick, G. M. *SHELXL-93. Program for Crystal Structure Refinement from Diffraction Data*; University of Göttingen, 1993]). The final *R*(*F*²) was 0.026 for observed data. The atomic coordinates, bond lengths and angles were deposited by CSD and can also be obtained in the form of the CIF file from the author (J.P.) by e-mail.
10. When this study was in progress, the crystal structure of (*RS*)-**2a** was independently determined: Gerkin, R. E. *Acta Crystallogr.* **1998**, *C54*, 1369.
11. The observed self-assembling pattern of the racemic diacid (*RS*)-**2a** is unexceptional. According to the Cambridge Database, linking of molecules of opposite chirality into infinite zig-zag chains by double hydrogen bonds is a common feature of racemic 2,2'-disubstituted biaryl-6,6'-dicarboxylic acids.
12. At concentrations higher than 0.15 mol kg⁻¹.