

**FORMATION OF INFINITE GRIDS WITH CHIRAL SQUARE
COMPARTMENTS BY SELF-ASSEMBLY OF ACHIRAL
1,1'-BIPHENYL-2,2',6,6'-TETRACARBOXYLIC ACIDS.⁺
EFFECT OF 4,4'-SUBSTITUTION ON THE GRID STACKING**

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The achiral 1,1'-biphenyl-2,2',6,6'-tetracarboxylic acid as well as its 4,4'-dibromo and 4,4'-dinitro derivative self-assemble in crystal under formation of a two-dimensional grid set up from hydrogen-bonded cyclotetrameric compartments which are individually chiral (D_4 symmetry). The roughly square cavities (ca 5.6 Å) of individual compartments partly accommodate the perpendicularly oriented benzene rings of the neighbouring grid, in dependence on the nature of the 4,4'-substituents. As a consequence, the grids are stacked in a staggered (nonconcatenated) manner.

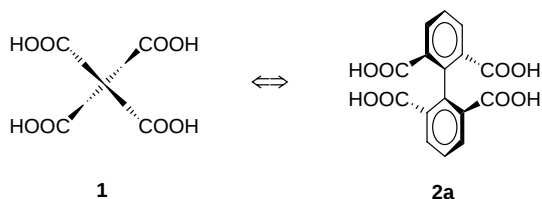
Keywords: Carboxylic acids; Crystal structure determination; Hydrogen bonds; Crystal engineering; Self assembly; Chiral porous solids; Biaryls; Biphenyls.

Supramolecular self-assembly is the spontaneous association of molecular subunits (tectons²) into ordered aggregates, which is driven by non-covalent interactions³, e.g. by intermolecular hydrogen bonds. Tetrafunctional molecules with tetrahedrally arranged substituents have been investigated in this context and have shown to exhibit the fascinating capability of building diamond-like networks⁴ with methanetetraacetic acid **1** being a prototypical example⁵.

We are interested in the self-assembly of 2,2',6,6'-tetrasubstituted biphenyls^{6,7} that are topologically related to the tetrasubstituted methanes: if we

+ Part of the results contained in this paper has been already communicated in a preliminary form¹.

stretch the D_{2d} symmetry conformer of the tecton **1** along its axis, a framework of 1,1'-biphenyl-2,2',6,6'-tetracarboxylic acid **2a** can be (on further synthetic elaboration) obtained (Scheme 1).



SCHEME 1
Stereochemical correlation of the tectons **1** and **2**

All the same, examination of models suggests that the self-assembling properties of the two stereochemically akin tectons **1** and **2a** can be entirely different. In contrast to the established propensity of the tetrahedral tecton **1** to form chair-like distorted cyclohexamers underlying the three-dimensional diamondoid network^{4,5}, models of the stretched tecton **2a** suggest a preferential cyclotetramerisation resulting ultimately in an infinite “square” grid (Fig. 1).

RESULTS AND DISCUSSION

In accord with the consideration of models, X-ray crystal structure determination of the parent (unsubstituted) acid **2a** exhibits an approximately perpendicular orientation of the phenyls in the individual molecules with the

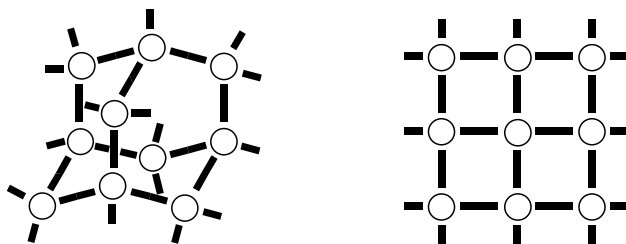


FIG. 1
Schematic representation of diamondoid and square grids

dihedral angle between the least squares planes of the benzene rings being $86.26(6)^\circ$ (Fig. 2). However, the pivot atoms of the substituents are displaced from the aromatic planes by as much as $0.190(3)$ Å for the perpendicular distance of C(11) from the plane defined by C(1) to C(6). The carboxyl groups, the hydrogen atoms of which were located and refined, are also essentially planar but adopt varying orientation relatively to their parent benzene rings: the dihedral angles of the carboxyl planes relatively to the adjoined aromatic rings are $8.1(4)^\circ$ for C(7), $35.1(3)^\circ$ for C(8), $14.2(3)^\circ$ for C(17) and $44.5(2)^\circ$ for C(18) carboxyl; the steric hindrance imposed by the crystal packing (*vide infra*) is assumed to be the responsible factor. All four carboxyl groups participate in the intermolecular hydrogen bonding. There are two crystallographically independent double hydrogen bonds, both nearly planar and with asymmetrically located hydrogen atoms: one links O(1) and O(2) with O(12') and O(11') and the other is between O(3), O(4) and O(14''), O(13''). These results in the formation of hydrogen-bonded cyclotetramers (Fig. 3), set up ultimately into an infinite quasi-planar "square" network (grid).

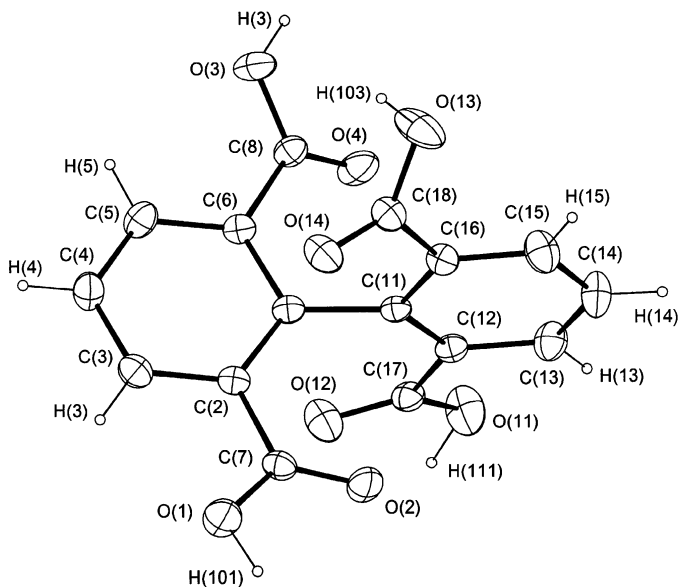


FIG. 2

An ORTEP diagram of the molecular structure of **2a** with the crystallographic numbering scheme

Stereochemistry of the cyclotetramers (“squares”) raises a particular interest. In contrast to the individual tectons **2a** that possess D_{2d} symmetry and are accordingly achiral, the self-assembled cyclotetramers exhibit (in an ideal arrangement) a unique^{8,9} D_4 symmetry and are therefore chiral. Homochiral cyclotetramers are arranged diagonally, whereas alternation of chirality occurs in the horizontal and vertical rows of the grid (Fig. 4). In contrast to the chirality of the individual cyclotetramers, the infinite unilayered grid is achiral due to the crystal symmetry.

The roughly square cavities inside the cyclotetrameric compartments are approximately 5.6 Å in size, which allows to accommodate partly the nearly perpendicularly oriented benzene rings of the neighbouring grids. As a consequence, the grids are stacked in a staggered (non-concatenated) manner (Fig. 3).

In order to assess a broader scope of this novel supramolecular architecture, we have examined the effect of substitution of the parent tecton **2a** on the crystal structure. To this end, three 4,4'-disubstituted derivatives, **2b–2d**, have been prepared. Bromination of **2a** in the presence of Ag^+ ions afforded the 4,4'-dibromo-substituted tetraacid **2b**. Similarly, nitration of **2a** yielded the 4,4'-dinitro-substituted tetraacid **2c**. The Ullmann coupling

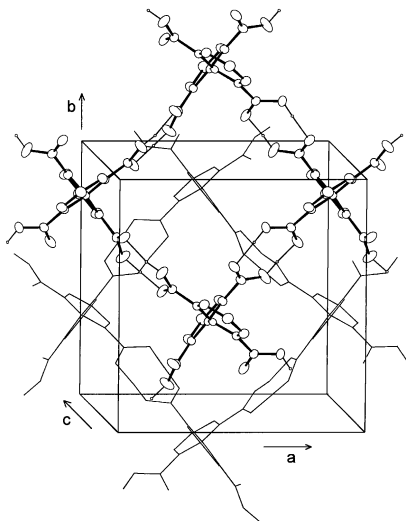
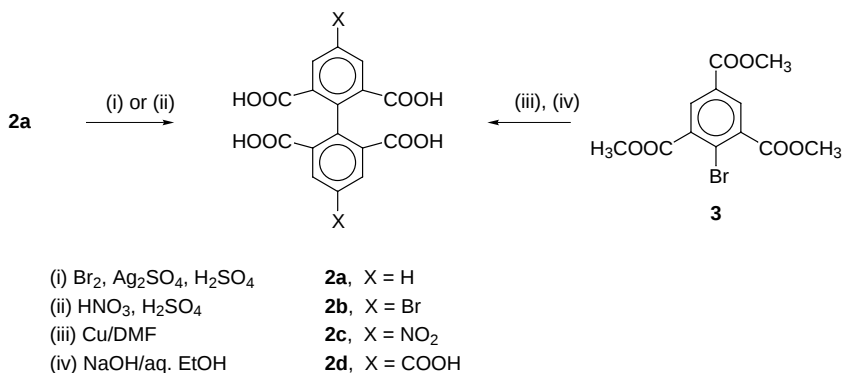


FIG. 3

Self-assembly of **2a** into unilayered hydrogen-bonded networks and stacking of the neighbouring layers in the crystal (the molecules in the second layer are distinguished by thinner lines)

of trimethyl 2-bromobenzene-1,3,5-tricarboxylate **3** with activated copper bronze followed by alkaline hydrolysis led to 1,1'-biphenyl-2,2',4,4',6,6'-hexacarboxylic acid **2d** (Scheme 2).



SCHEME 2

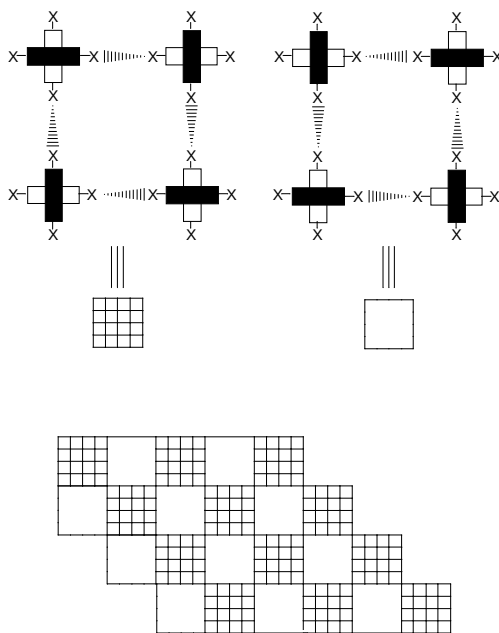


FIG. 4

Schematic representation of the distribution of cyclotetramers of opposite chirality (indicated by empty and filled squares) in the unilayered hydrogen-bonded network in the crystal of **2a**

The molecular structure of the dibromo-substituted tetraacid **2b** is given in Fig. 5. The molecule resides on a crystallographic two-fold axis passing through the midpoint between the Br atoms. The benzene rings are planar within ± 0.010 Å and are arranged almost perpendicularly to the dihedral angle of the least-squares planes of $85.6(1)^\circ$. In contrast to the parent tetraacid **2a**, the pivot atoms of the substituents are displaced only very slightly from the benzene plane, the greatest deviation being $0.023(7)$ Å for C(7). The tilting of the carboxyl groups relatively to the benzene plane is $17.8(7)^\circ$ and $13.3(9)^\circ$ for C(7)–O(1)–O(2) and C(8)–O(3)–O(4), respectively. In the unsubstituted tetraacid **2a**, the analogous dihedral angles of the four independent carboxyl groups span the much broader range of 8.1 – 44.5° . The carboxyl groups in **2b** are linked by short (O $\cdots$ O 2.601–2.616 Å), slightly bent (angles at hydrogen atoms being $163(7)^\circ$ and $164(6)^\circ$) and markedly asymmetric intermolecular double hydrogen bonds, giving rise to the already known (*vide supra*) two-dimensional “square” layers propagating diagonally through the unit cell (Fig. 6). The staggered stacking of these layers allows to partly interpenetrate each other, however, less effectively than in the unsubstituted compound **2a**. Assumedly, the van der Waals contacts of bromine atoms belonging to molecules two layers apart are the responsible factor that prevents the adjacent layers to become closer than 8.2 Å; the corresponding distance in the unsubstituted derivative is 5.28 Å.

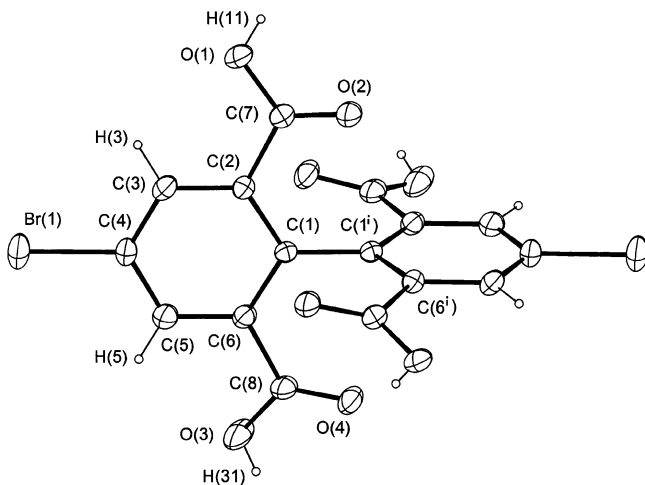


FIG. 5

An ORTEP diagram of the molecular structure of **2b** with the crystallographic numbering scheme. Symmetry code: i, $1 - x, y, 0.5 - z$

The crystal structure of the dinitro-substituted tetraacid **2c** involves two crystallographically independent molecules A and B differing in their conformation, in particular in the degree of bending of the benzene rings away from the idealised two-fold axis. In all other aspects, the molecules A and B are very similar. The perspective view of molecule A is given in Fig. 7; for

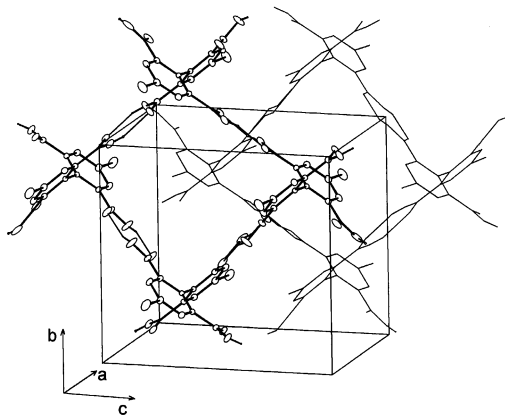


FIG. 6

Self-assembly of **2b** into unilayered hydrogen-bonded networks and stacking of the neighbouring layers in the crystal (the molecules in the second layer are distinguished by thinner lines)

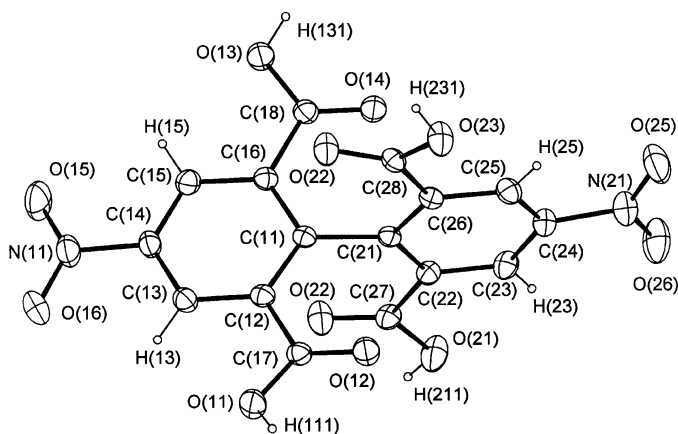


FIG. 7

An ORTEP diagram of one crystallographically independent molecule of **2c** with the numbering scheme. For the second molecule, add 2 to the first digit of the atom labels

molecule B, add 2 to the first digit of the atom labels. The benzene rings in each molecule are arranged almost perpendicularly, the appropriate least squares planes subtending the dihedral angle of $89.70(9)^\circ$ and $89.17(9)^\circ$ for molecules A and B, respectively. Compared to the unsubstituted tetracarboxylic acid **2a**, the most conspicuous difference is the almost coplanar arrangement of the carboxyl groups with the adjacent benzene planes; the largest deviation from coplanarity is $16.4(1)^\circ$, in a close analogy with the situation found for the dibromo-substituted tecton **2b**.

In the crystal of the compound **2c**, there are two kinds of intermolecular interaction. The first is common for the tectons **2a–2c**: short, double hydrogen bond bridges between the carboxyl groups link the molecules into two-dimensional “square” grids stacked in a staggered manner, allowing the individual layers to partly penetrate (Fig. 8). Considering the two independent molecules A and B, the grids defined by the centroids of the molecules are arranged into ABAB rows and in alternating AAA and BBB columns. In contrast to the crystal structure of **2a** and **2b**, in which the centroids within each layer are coplanar due to crystal symmetry, the grid in the dinitro derivative **2c** is puckered: the angles of the intercentroid links are $166.9(2)^\circ$ along the ABAB direction, $178.7(2)^\circ$ along AAA and $175.8(2)^\circ$ along BBB. This appears to be the consequence of the second type of the

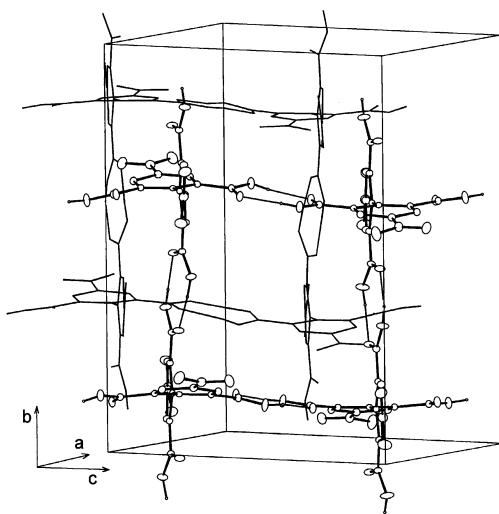


FIG. 8

View of the staggered grids in **2c** resulting by hydrogen bonding. Secondary chains formed by stacking of the nitro groups run approximately parallel to the grids

intermolecular interaction, which in the investigated series is specific for the nitro substituent. Because of the zig-zag arrangement of the ABAB rows, their peripheral nitro groups come into close contacts with the nitro groups of the molecules which are two layers apart. Due to the presence of two independent molecules, there are two such interactions between the translationally related nitro substituents of A and B: N(11) to N(41) ($x - 1, y, z$), distance of the centroids of the nitro groups 3.141(3) Å, dihedral angle of the NO₂ planes 1.0(1)°; N(21) to N(31) ($x, y, 1 - z$), 3.085 Å, 3.19(9)°. This NO₂-stacking links the molecules into secondary chains which are approximately perpendicular to the layers formed by the hydrogen bonding. The assumption that this stacking accounts for the deformation of the grid from planarity is supported by the fact that the links of the centroids are almost linear within the columns of the AAA and BBB type, which lack any secondary NO₂ interaction perpendicular to the direction of the column.

Intermolecular stacking of aromatic nitro groups is, of course, a common phenomenon and almost thousand cases has been retrieved from the Cambridge Structural Database for the absolute value of the dihedral angle limited to 10° and the intercentroid distance up to 4.5 Å. However, the mean of the (non-Gaussian) distribution of the distances reaches 3.586 Å and the values shorter than 3.2 Å represent less than 7% of the total. In the present structure, the strong interaction of the nitro groups allows the layers to interpenetrate more effectively than in the dibromo derivative **2b**, in spite of the formal van der Waals diameter of the nitro group (assuming its free rotation) which is larger than that of the bromo substituent.

Irrespective of the specific (relatively minor) substituent effect, uniform pattern in the solid-state self-assembly of the biphenyl tectons **2a–2c** has been in this way established. Structure tuning of the novel supramolecular architecture remains nevertheless on the agenda. First, the effective size of the individual “square” compartments should be expanded, employing appropriate spacers. Next, chirality of the individual “squares” should be extended to the overall network (grid) by the use of appropriate chiral tectons¹⁰. Lastly, stacking of the individual grids should be examined in a more detail. Although the staggered stacking has now been shown in the tectons **2a–2c** to be a “normal” outcome of the self-assembly, enforcement of the alternative, eclipsed stacking stands as a challenging task. Introduction of appropriate “sticking” substituents into the 4,4'-positions of the biphenyl tecton might be instrumental¹¹ in this respect, allowing formation of an additional (perpendicular) network of intermolecular non-covalent bonds. We have therefore introduced “sticking” 4,4'-carboxyl groups into the tecton **2d** as the first probe; unfortunately, we have failed

to grow a suitable crystal. Further studies along these lines which ultimately could lead to the design of chiral porous solids¹² are in progress.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. ¹H NMR spectra were measured on a Varian Unity XL-200 spectrometer (200 MHz, FT mode) using tetramethylsilane as an internal standard. Mass spectra were recorded on a ZAB-EQ (VG Analytical) instrument, for FAB technique thioglycerol/glycerol matrices were used. Chemical shifts are given in ppm (δ -scale).

4,4'-Dibromo-1,1'-biphenyl-2,2',6,6'-tetracarboxylic Acid (**2b**)

To a stirred mixture of the unsubstituted¹ tetraacid **2a** (3.30 g, 10 mmol) and silver(I) sulfate¹³ (3.43 g, 11 mmol) in concentrated sulfuric acid (98%, 40 ml), bromine (3.52 g, 22 mmol) was added dropwise at 120 °C (0.5 h). After additional 4 h heating, the cooled mixture was poured onto crushed ice (200 g). The yellow precipitate was filtered off, washed with cold water and suspended in a saturated aqueous solution of NaHCO₃ (2 × 50 ml). The insoluble silver salt was filtered off and the filtrate was acidified to pH 1 with concentrated HCl. The precipitated product was collected and recrystallised from hot water. Yield 3.55 g (73 %), m.p. >370 °C. ¹H NMR (DMSO-*d*₆): 8.13 s, 4 H (H-3,3',5,5'); 12.95 br s, 4 H (4 × COOH). FAB MS, *m/z* (rel.%): 491 (MH⁺, 10), 489 (MH⁺, 20), 487 (MH⁺, 10), 473 (13), 471 (26), 469 (13), 201 (33), 181 (21), 149 (15), 115 (25), 110 (36), 91 (100), 75 (73), 73 (70), 57 (73). For C₁₆H₈Br₂O₈ (488.0) calculated: 39.38% C, 1.65% H, 32.74% Br; found: 39.56% C, 1.60% H, 32.76% Br.

4,4'-Dinitro-1,1'-biphenyl-2,2',6,6'-tetracarboxylic Acid (**2c**)

A mixture of the unsubstituted¹ tetraacid **2a** (3.30 g, 10 mmol), nitric acid (65%, 20 ml) and concentrated sulfuric acid (98%, 20 ml) was heated at 120 °C under stirring for 4 h. After cooling, the mixture was poured onto crushed ice (200 g). The precipitated product was filtered off and recrystallised from hot water. Yield 3.05 g (73%), m.p. >370 °C. ¹H NMR (DMSO-*d*₆): 8.79 s, 4 H (H-3,3',5,5'); 13.43 br s, 4 H (4 × COOH). EI MS, *m/z* (rel.%): 420 (M⁺, 20), 331 (31), 313 (14), 288 (20), 287 (100), 250 (21), 126 (15), 69 (14), 57 (18), 55 (16), 44 (21), 43(20). For C₁₆H₈N₂O₁₂ (420.3) calculated: 45.73% C, 1.92% H, 6.67% N; found: 46.09% C, 1.86% H, 6.38% N.

1,1'-Biphenyl-2,2',4,4',6,6'-hexacarboxylic Acid (**2d**)

A stirred mixture of the triester **3** (3.31 g, 10 mmol) and activated copper bronze¹⁴ (2.5 g) in dimethylformamide (15 ml) was heated at 150 °C under argon for 1 h, then poured into water (100 ml) and extracted with ethyl acetate (3 × 20 ml). The combined extracts were dried with anhydrous MgSO₄, filtered and evaporated to dryness. The solid residue was dissolved in of hot methanol (100 ml). After cooling the crystals of the resulting hexamethyl ester were collected, washed by methanol and dried. Yield 1.85 g (73.6%), m.p. 212–214 °C. ¹H NMR (CDCl₃): 8.85 s, 4 H (H-3,3',5,5'); 3.99 s, 12 H (CH₃-2,2',6,6'); 3.65 s, 6 H (CH₃-4,4'). EI MS, *m/z* (rel.%): 502 (M⁺, 100), 471 (73), 443 (32), 427 (38), 381 (28), 369 (12), 220 (19),

7 (16), 57 (21). For $C_{24}H_{22}O_{12}$ (502.4) calculated: 57.37% C, 4.41% H; found: 57.18% C, 4.36% H.

The hexaester (1.17 g, 2.33 mmol) was saponified by sodium hydroxide (0.836 g, 21 mmol) in 70% aqueous ethanol (25 ml). After 6 h reflux, the mixture was acidified to pH 1 with 2 M HCl and solvents were evaporated. The residue was crystallised from hot water (100 ml). Yield 0.82 g (84.2%), m.p. >370 °C. 1H NMR (DMSO- d_6): 8.55 s, 4 H (H-3,3',5,5'); 10.95 br s, 6 H ($6 \times COOH$). FAB MS, m/z (rel.%): 419 (MH^+ , 16), 401 (29), 307 (20), 232 (17), 215 (100), 214 (62), 197 (75), 181 (45), 165 (23), 149 (33), 133 (30), 123 (48), 110 (68). For $C_{18}H_{10}O_{12}$ (418.3) calculated: 51.69% C, 2.41% H; found: 51.56% C, 2.44% H.

Trimethyl 2-Bromobenzene-1,3,5-tricarboxylate (**3**)

To a stirred mixture of 2-bromomesitylene (21.2 g, 0.106 mol) and aqueous NaOH (5.5 g, 0.1375 mol, 500 ml H_2O) under reflux solid $KMnO_4$ (112g, 0.709 mol) was added portionwise during 4 h. After additional 4 h heating, the excess of $KMnO_4$ was removed by several drops of formaline, the mixture was filtered and the separated MnO_2 was washed with hot water. The filtrate and washings were combined, concentrated to 100 ml and acidified to pH 1 with concentrated HCl. The deposited triacid was isolated by filtration, washed with little water and dried. Yield 19.3 g (63.0%), m.p. 291–294 °C; ref.¹⁵ 260–275 °C.

The crude acid was suspended in methanol (700 ml), concentrated sulfuric acid (20 ml) was added and the mixture was heated to reflux for 20 h. The volume was reduced to 200 ml and cooled in a refrigerator. The resulting triester was filtered off, washed with a small volume of methanol and dried. Yield 18.7 g (84.6%), m.p. 93–95 °C. 1H NMR (DMSO- d_6): 8.35 s, 2 H (H-3,5); 3.98 s, 6 H (CH_3 -2,6); 3.96 s, 3 H (CH_3 -4). EI MS, m/z (rel.%): 332 (M^+ , 42), 330 (M^+ , 43), 301 (98), 299 (100), 258 (8), 256 (8), 227 (8), 225 (8), 177 (11), 115 (25), 74 (15), 59 (7). For $C_{12}H_{11}BrO_6$ (331.1) calculated: 43.53% C, 3.35% H, 24.13% Br; found: 43.80% C, 3.36% H, 24.29% Br.

Single-Crystal X-Ray Diffraction

All measurements have been performed on a CAD4 diffractometer at 293(2) K (MoK α radiation, $\lambda = 0.710073$ Å).

2a: $C_{16}H_{10}O_8$, $M = 330.24$, orthorhombic, space group $Pbca$ (No. 61), $a = 11.862(2)$ Å, $b = 12.098(1)$ Å, $c = 21.0333(2)$ Å, $V = 3018.4(6)$ Å³, $F(000) = 1\ 360$, $D_c = 1.453$ g cm⁻³ for $Z = 8$. A colourless plate of the dimensions $0.30 \times 0.19 \times 0.11$ mm was grown from hot water by slow cooling. From a total of 2 361 reflections measured in the range $h = 0$ to 13, $k = 0$ to 13, $l = 0$ to 24, 1 642 were regarded as observed according to the $I > 2\sigma(I)$ criterion. Absorption was neglected ($\mu = 0.119$ mm⁻¹). The structure was solved by direct methods (SHELXS86)¹⁶ and refined by full-matrix least squares based on F^2 (SHELXL93)¹⁷. The O-bonded hydrogen atoms were refined isotropically, the C-bonded hydrogens were fixed in calculated positions and assigned the temperature parameters amounting to 1.2-multiples of those of their bonding partners. The refinement converged to $R = 0.0383$, $wR = 0.0874$, $GOF = 1.042$ for 233 parameters. The final difference map displayed no peaks of chemical significance.

2b: $C_{16}H_8Br_2O_8$, $M = 488.04$, monoclinic, space group $C2/c$ (No. 15), $a = 13.633(1)$ Å, $b = 11.160(1)$ Å, $c = 12.7769(9)$ Å, $\beta = 101.694(6)^\circ$, $V = 1903.6(6)$ Å³, $F(000) = 1\ 088$, $D_c = 1.703$ g cm⁻³ for $Z = 4$. A colourless irregular block of the dimensions $0.10 \times 0.12 \times 0.13$ mm was grown from aqueous ethanol. From a total of 1 738 reflections measured in the range

$h = 0$ to 16, $k = 0$ to 13, $l = -15$ to 14, 1 671 were independent ($R_{\text{int}} = 0.019$) and 1 176 were regarded as observed according to the $I > 2\sigma(I)$ criterion. Three standard reflections monitored every 1 h showed 2.7% total decay. The intensities were corrected for absorption ($\mu = 0.140 \text{ mm}^{-1}$) by a numerical method¹⁸ ($T_{\text{min}} = 0.4249, 0.5607$). The structure was solved by direct methods (SIR3)¹⁹ and refined by full-matrix least squares based on F^2 (SHELXL93)¹⁷. The aromatic hydrogens were fixed in calculated positions and assigned the temperature parameters amounting to 1.2-multiples of those of their bonding partners; the carboxyl hydrogens were refined isotropically. The refinement converged to $R = 0.0456$, $wR = 0.1020$, $GOF = 1.069$ for 126 parameters. The final difference map displayed no peaks of chemical significance.

2c: $\text{C}_{16}\text{H}_8\text{N}_2\text{O}_{12}$, $M = 437.38$, monoclinic, space group $P2_1/c$ (No. 14), $a = 14.684(2) \text{ \AA}$, $b = 16.993(1) \text{ \AA}$, $c = 15.470(2) \text{ \AA}$, $\beta = 111.812(9)^\circ$, $V = 3583.3(7) \text{ \AA}^3$, $F(000) = 1\ 848$, $D_c = 1.621 \text{ g cm}^{-3}$ for $Z = 8$. A colourless irregular prism of the dimensions $0.35 \times 0.40 \times 0.40 \text{ mm}$ was selected from the preparative batch. From a total of 5 852 reflections measured in the range $h = 0$ to 16, $k = 0$ to 19, $l = -17$ to 16, 5 614 were independent ($R_{\text{int}} = 0.013$) and 3 647 were regarded as observed according to the $I > 2\sigma(I)$ criterion. Three standard reflections monitored every 1 h showed 2.9% total decay. The structure was solved by direct methods (SIR3)¹⁹ and refined by full-matrix least squares based on F^2 (SHELXL93)¹⁷. The aromatic hydrogens were fixed in calculated positions and assigned the temperature parameters amounting to 1.2-multiples of those of their bonding partners; the carboxyl hydrogens were refined isotropically. The refinement converged to $R = 0.0435$, $wR = 0.1154$, $GOF = 1.030$ for 573 parameters. The final difference map displayed no peaks of chemical significance.

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-102374 (**2a**), CCDC-152285 (**2b**) and CCDC-152286 (**2c**). Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

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8. Eliel E. L., Wilen S. H., Mander L. N.: *Stereochemistry of Organic Compounds*, p. 79. Wiley, New York 1994.
9. According to E. L. Eliel⁸, no organic molecules of D_4 symmetry have yet been synthesised. Also, to our best knowledge, no hydrogen-bond-organised substructure of D_4 symmetry has been found in any previously known crystal structure.
10. Two pertinent examples of chiral "square" grids based on homochiral 2,2',6,6'-tetra-substituted biaryls have been already reported; refs^{6,7}.
11. However, "sticking" substituents are not *conditio sine qua non*; one case of an unsupported eclipsed stacking of a homochiral 2,2',6,6'-tetrasubstituted biaryl has been already reported, giving rise to set-up of chiral columns from the hydrogen-bonded cyclotetrameric "squares"; ref.⁷.
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