

**SELF-ASSEMBLY OF 1,1'-BIPHENYL-2,2',6,6'-TETRACARBOXAMIDES.
EFFECT OF SUBSTITUTION AT THE AMIDIC NITROGEN**Petr HOLÝ^{a1}, Jaroslav PODLAHA^b, Ivana ČISAŘOVÁ^{b1} and Jiří ZÁVADA^{a2,*}^a Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 166 10 Prague 6, Czech Republic; e-mail: ¹ petrholy@uochb.cas.cz, ² zavada@uochb.cas.cz^b Department of Inorganic Chemistry, Charles University, 128 40 Prague 2, Czech Republic; e-mail: ¹ cisarova@prfdec.natur.cuni.cz

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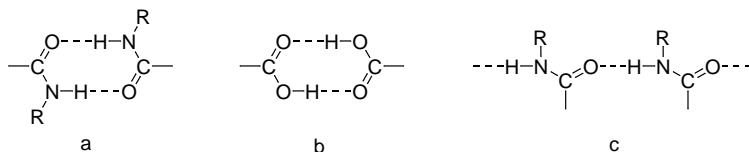
Self-assembly of three 1,1'-biphenyl-2,2',6,6'-tetracarboxamides **2a–2c** differing each from the other by substitution at the amidic nitrogens (R = H, ethyl and 1-(*R*)-phenylethyl, respectively) was investigated by single crystal X-ray diffraction analysis. It was found that the unsubstituted tetracarboxamide **2a** gives rise to infinite hydrogen-bonded 2D network composed from chiral cyclotetrameric squares (D_4 symmetry). Such self-assembling pattern is suppressed by alkyl substitution in **2b** and **2c**, which disfavors formation of intermolecular amide–amide hydrogen bonds.

Keywords: Amides; Crystal structure determination; Hydrogen bonds; X-Ray diffraction; Crystal engineering; Solid state self-assembly; Biaryls; Biphenyls; Supramolecular structures.

Recently¹, we have demonstrated that solid-state self-assembly of 1,1'-biphenyl-2,2',6,6'-tetracarboxylic acid **1** gives rise to a novel type of supramolecular architecture. Intermolecular double hydrogen bonds between the carboxyl groups placed on the orthogonal biphenyl framework lead to the formation of an infinite 2D network which is set up from square-like cyclotetrameric compartments (Fig. 1). In contrast to the single tetraacid molecules, which possess the D_{2d} symmetry and are accordingly achiral, the cyclotetramers exhibit unique^{2,3} D_4 symmetry being thus individually chiral. Homochiral cyclotetramers are arranged diagonally, whereas alternation of chirality occurs in the horizontal and vertical rows of the hydrogen-bonded network. Such stereochemically unusual self-assembly continues^{4–6} to stimulate our interest.

In order to assess steric requirements of this self-assembling pattern, we have now examined the single crystal structure of three 1,1'-biphenyl-2,2',6,6'-tetracarboxamides **2a–2c** each differing from the other by bulkiness of the substituent on the nitrogen atoms. Amides are known for their capa-

bility of forming intermolecular hydrogen bonds. Primary amides^{7,8} as a rule give rise to double hydrogen bonds (Scheme 1a), analogously to carboxylic acids⁸ (Scheme 1b), whereas secondary amides⁹⁻¹² are usually engaged in formation of single hydrogen bonds (Scheme 1c).



SCHEME 1

As we have shown earlier, single⁵ as well as double^{1,4,6} hydrogen bonds allow self-assembly of 2,2',6,6'-tetrasubstituted biaryls into chiral cyclo-tetrameric squares.

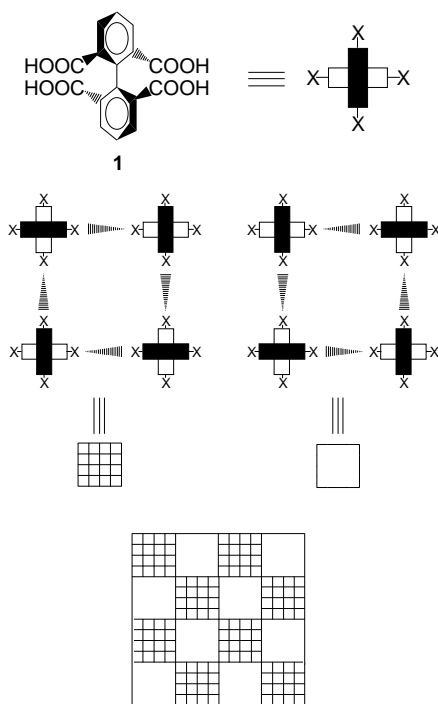


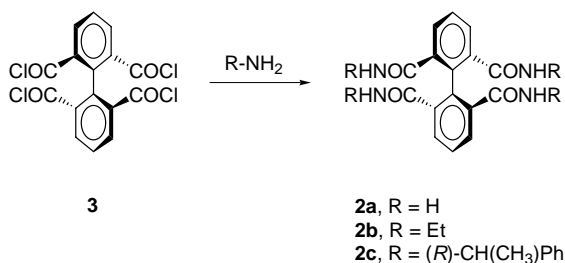
FIG. 1

Schematic representation of the stepwise self-assembly of **1** into hydrogen-bonded network

RESULTS AND DISCUSSION

Syntheses of Tetracarboxamides 2a–2c

All tetracarboxamides were prepared simply by the reaction of 1,1'-biphenyl-2,2',6,6'-tetrakis(carbonylchloride)^{13,14} **3** with an appropriate amine (Scheme 2).



SCHEME 2

Crystal Structure of Unsubstituted Tetracarboxamide 2a

The asymmetric unit consists of two molecules of tetraamide **2a** (A, B) and one disordered molecule of water. A perspective view of the molecule A is depicted in Fig. 2, from which the system of atom labelling is also evident.

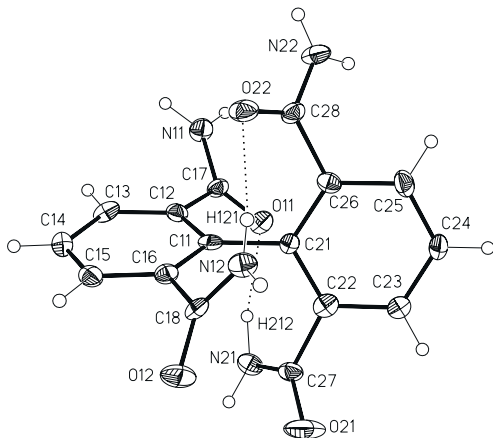


FIG. 2

Perspective view of one of the two independent molecules of the tetraamide **2a** (thermal ellipsoids at the 50% probability level) with atom labeling. For the second molecule, add 2 to the first digit of atom label. Intramolecular hydrogen bonds are shown as dotted lines

Superposition of molecules A and B shows a close similarity of their geometries, mostly within standard deviation of the corresponding parameters (bond distances and angles) which are unexceptional and deserve no comment. The mean planes of the benzene rings subtend dihedral angles of $74.6(2)$ and $74.9(2)^\circ$ for molecules A and B, respectively; the pivot atoms of the amide groups are displaced from these planes by as much as $0.180(9)$ Å for C17 and are tilted relative to the aromatic ring by 46.1 – 56.7° . In the crystal, the molecules are linked by *double intermolecular hydrogen bonds* between amide groups. There are four double hydrogen bonds linking each molecule A to four molecules B and *vice versa*. Further, there are two *single intermolecular hydrogen bonds*, which link separately molecules A and molecules B into zig-zag chains (Fig. 3a). Ten of the total sixteen amide hydro-

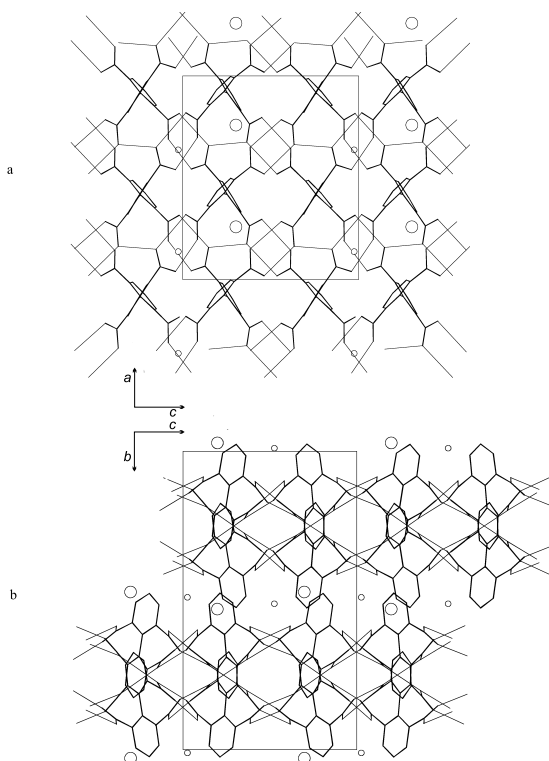


FIG. 3

Two views of the unit cell content of tetraamide **2a** showing the double layer projected on the *ac* plane (a) and stacking of these layers along the *b* axis (b). The disordered water molecules, which separate the layers, are depicted as large and small circles according to their relative population

gens in the asymmetric unit participate in the intermolecular bonding giving rise to an infinite two-dimensional grid, which in the third dimension is two-molecules thick. On close analysis, this arrangement consists of two parallel (one-molecule thick) layers, which are held together by a system of single hydrogen bonds. Each of the two interconnected layers is composed of cyclotrameric compartments which are held together by double hydrogen bonds. The double layers are stacked in the crystallographic *b*-direction, leaving space around *b*/2 which accommodates the disordered water molecules (Fig. 3b) held by further hydrogen bonds, albeit poorly defined because of the disorder. Two individual positions of the disordered water (70 : 30 in rel.% occupancy) differ in the type of this bonding, the major one being acceptor of the amide proton from N22 and the minor one donor of its hydrogen to O21. The intermolecular links are complemented by *intramolecular single hydrogen bonds* pairwise connecting amide groups at different phenyls in the individual molecules (Fig. 2). In asymmetric unit, four amide hydrogens participate in this intramolecular bonding.

Crystal Structure of N,N',N'',N'''-Tetraethyl Substituted Tetracarboxamide 2b

Its molecular structure consists of two symmetry-dependent halves, which are related by the crystallographic C_2 axis passing through the midpoint of the C1-C1' bond (Fig. 4). The orientation of the phenyl group to this axis results in the dihedral angle of $76.1(1)^\circ$ between the mean-least squares planes of the two symmetry-related phenyl groups. The benzene ring is planar within ± 0.020 Å but the pivot atoms of its substituents are displaced from this plane by $0.027(3)$ Å for C1', $-0.085(3)$ Å for C7, and even $0.183(3)$ Å for C10. The crystallographically independent *N*-ethyl groups have slightly different conformation; their dihedral angles to the benzene plane being $58.3(4)^\circ$ for C7(O1)N1H1 and $53.4(3)^\circ$ for C10(O2)N2H2. However, the four atoms of both amide groups are coplanar within at least ± 0.014 Å. The amide groups on the opposite phenyls are linked by an *intramolecular N-H...O* single hydrogen bond (Fig. 4). *Intermolecular association takes place only with the participation of water molecules* (Fig. 5). The carbonyl groups act as acceptors of hydrogen atoms from water molecules that are of two kinds: the O3 atom donates its second hydrogen atom (not involved in bonding to carbonyl) to O4, which is located on the two-fold axis. The result is a bent dicoordination at O1, an approximately planar coordination at O2 and O3 and a distorted tetrahedron at O4. This system of hydrogen bonding links

the individual molecules along the crystallographic *ab* plane into two-dimensional layers, which are stacked along the *c* axis at van der Waals distances.

Crystal Structure of N,N',N'',N'''-Tetra((R)-1-phenylethyl) Substituted Tetracarboxamide 2c

Its molecular structure is depicted in Fig. 6. It is composed of two symmetry-dependent halves related by the two-fold axis through C4, C1, C21 and C24 atoms. The phenyl groups are all planar within $\pm 0.0014 \text{ \AA}$ and the biphenyl rings are arranged at the dihedral angle of $79.5(1)^\circ$. Conformation of the crystallographically independent amide groups is markedly different, evidently because of the crowding imposed by the bulky 1-phenylethyl substituent. There are two *intramolecular single hydrogen bonds* between the amide hydrogen and the carbonyl oxygen on the neighbouring phenyl (Fig. 6). In contrast, *there is no intermolecular hydrogen bonding*. In the crystal, the molecules are packed at van der Waals distances and arranged along the

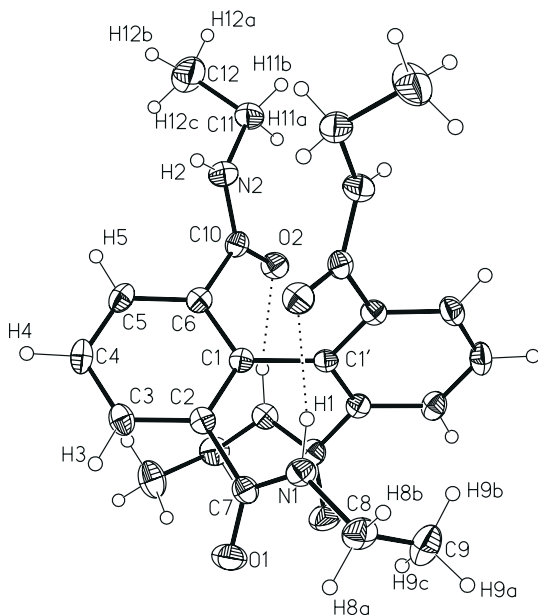


FIG. 4

Perspective view of the molecule of tetraamide **2b** (thermal ellipsoids at the 50% probability level) with atom labeling. Hydrogen bonds shown as dotted lines

hexagonal screw axis running in the crystallographic c direction (Fig. 7). This type of packing leaves channels along the axis¹⁵ located at 0,0, 0,1 and 1,0, where the disordered molecules of methanol are clathrated. The methanol molecules have no close contacts with the host molecules, in accordance with the observed fast deterioration of the crystals when dried at room temperature.

In this way, the fundamentally different results obtained for the three related tetracarboxamides **2a–2c** demonstrate the dramatic effect of the nitrogen substituents on their supramolecular self-assembly. The parent **2a**, which is sterically unshielded ($R = H$) exhibits analogous self-assembling pattern, as we found previously¹ for the corresponding tetracarboxylic

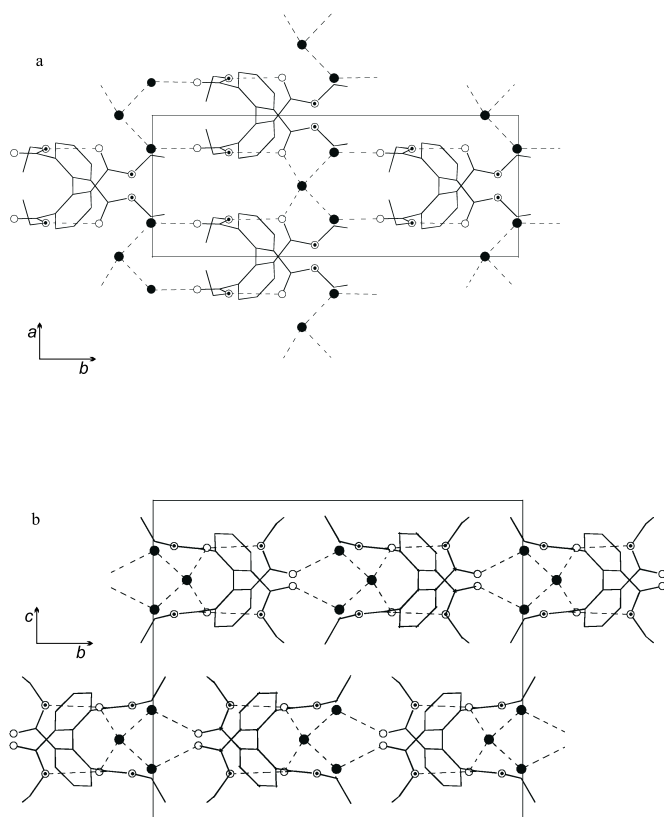


FIG. 5

Two projections of crystal packing of tetraamide **2b** with hydrogen bonds drawn as dashed lines. Atoms: ● water oxygen, ○ carbonyl oxygen, ⊙ nitrogen

acid **1**, *i.e.*, formation of infinite network set up from chiral hydrogen-bonded cyclotetrameric squares (Fig. 3a). Minor differences which exist between the two compounds may be accounted for by ability of tetraamide **2a** to complement the intermolecular hydrogen bonds with additional intramolecular bonds, pairwise connecting amide groups at the biphenyl (Fig. 2). Introduction of alkyl substituents on the amide nitrogen atoms ($R = \text{ethyl}$ or 1-phenylethyl) diminishes the number of available hydrogen bond donors. The observed absence of the intermolecular direct amide–amide hydrogen bonds in the crystal structure of **2b** and **2c** may thus be interpreted as resulting from the preferential (sterically less hindered) formation of the competing intramolecular amide–amide hydrogen bond.

In the self-assembly of the less shielded alkyl substituted tetraamide **2b** ($R = \text{Et}$), the direct amide–amide intermolecular linkage is replaced with water molecules coordinating to the neighbouring amide carbonyls. In the crystal of the more shielded derivative **2c**, even the undirect linkage (with participation of water molecules) is absent, most probably for steric reasons.

The absence of the intermolecular interactions assumedly accounts for the high solubility of the tetraamide **2c** in non-polar solvents (hexane,

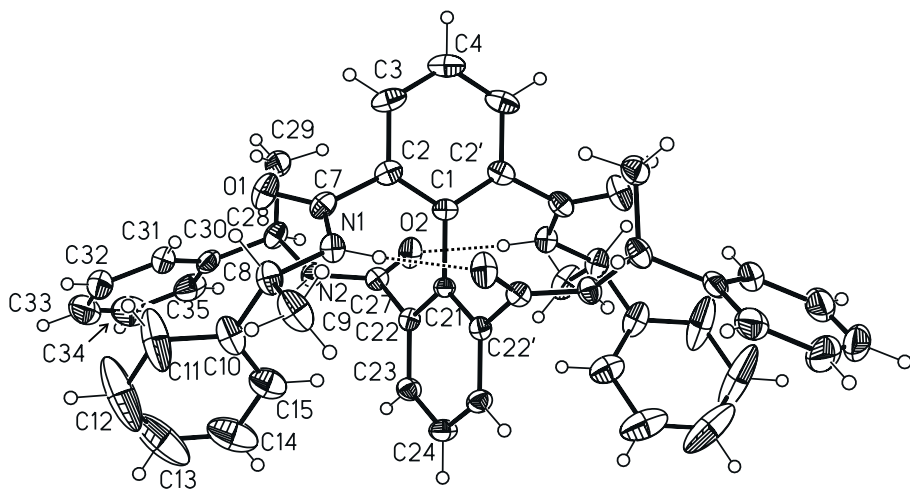


FIG. 6

Perspective view of the molecule of tetraamide **2c** (thermal ellipsoids at the 30% probability level) with atom labeling. Hydrogen bonds shown as dotted lines

CCl_4) as well as for remarkable volatility of this high molecular weight substance. Such peculiar behaviour was already noted by Prelog¹³ and interpreted tentatively in terms of intramolecular hydrogen bonding. Contrary to the original Prelog suggestion that four intramolecular hydrogen bonds are in the molecule of **2c**, only two bonds have now been found to exist in the single crystal.

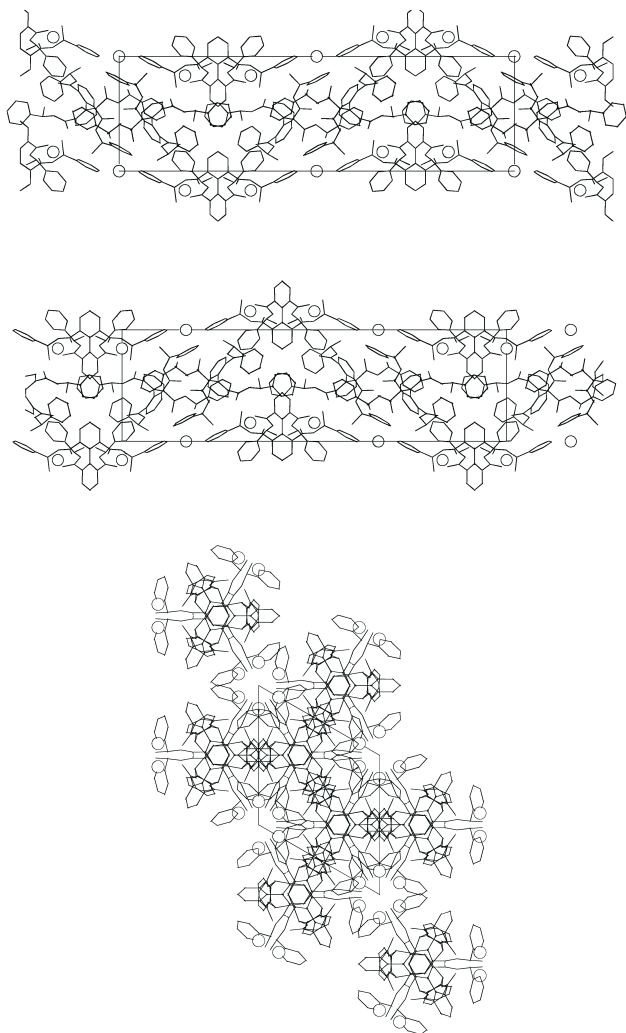


FIG. 7

Projections of crystal packing of tetraamide **2c** along three crystallographic axes. Disordered methanol is depicted as a circle at the centre of gravity of its molecule

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter; $[\alpha]_D$ values are given in 10^{-1} deg $\text{cm}^2 \text{g}^{-1}$. ^1H NMR spectra were measured on a Varian Unity XL-200 spectrometer (200 MHz, FT mode) using tetramethylsilane as an internal standard. Chemical shifts are given in ppm (δ -scale) coupling constants (J) in Hz. Mass spectra were recorded on a ZAB-EQ (VG Analytical) instrument.

1,1'-Biphenyl-2,2',6,6'-tetracarboxamide (2a)

A solution of tetrachloride¹⁶ **3** (380 mg, 0.94 mmol) in dioxane (15 ml) was dropped under stirring into concentrated aqueous ammonium hydroxide (25%, 10 ml) at 0 °C. After 20 min stirring the reaction mixture was evaporated to dryness and the solid residue was crystallized from hot water. Yield 280 mg (88.8%) of white crystals, m.p. 353–355 °C. ^1H NMR (DMSO- d_6): 7.96 br s, 4 H ($4 \times \text{CONH}$); 7.4–7.5 m, 6 H (arom. CH); 7.16 br s, 4 H ($4 \times \text{CONH}$). EI MS (m/z , rel.%): 326 (M^+ , 4), 282 (35), 265 (100), 239 (24), 222 (37), 97 (32), 85 (31), 83 (37), 57 (18), 71 (36), 69 (44), 57 (43), 55 (42), 43 (32). For $\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}_4 \cdot 0.5\text{H}_2\text{O}$ (326.3) calculated: 57.31% C, 4.51% H, 16.71% N; found: 56.96% C, 4.51% H, 16.51% N.

***N,N',N'',N'''*-Tetraethyl-1,1'-biphenyl-2,2',6,6'-tetracarboxamide (2b)**

Prepared from tetrachloride¹⁶ **3** (300 mg, 0.74 mmol) and 70% aqueous solution of ethylamine (10 ml) by an analogous procedure described for tetraamide **2a**. Crystallization from aqueous ethanol afforded 252 mg (69.3%) of the product (trihydrate), m.p. 184–185 °C. An analytical sample was recrystallized from heptane; m.p. 167–168 °C. ^1H NMR (CDCl_3): 7.46–7.60 m, 4 H ($4 \times \text{CONH}$); 7.44–7.46 m, 6 H (arom. CH); 3.05–3.23 m, 8 H ($4 \times \text{CH}_2$); 0.83 t, 12 H, $J(\text{CH}_3, \text{CH}_2) = 7.2$ ($4 \times \text{CH}_3$). EI MS (m/z , rel.%): 438 (M^+ , 100), 394 (12), 367 (31), 321 (14), 310 (29), 296 (49), 278 (40), 252 (29), 232 (42), 224 (37), 204 (25), 29 (16). For $\text{C}_{24}\text{H}_{30}\text{N}_4\text{O}_4$ (438.5) calculated: 65.73% C, 6.90% H, 12.78% N; found: 65.62% C, 6.87% H, 12.51% N.

***N,N',N'',N'''*-Tetrakis[(*R*)-1-phenylethyl]-1,1'-biphenyl-2,2',6,6'-tetracarboxamide (2c)**

Tetrachloride¹⁶ **3** (250 mg, 0.62 mmol) and (*R*)-1-phenylethylamine (500 mg, 4.13 mmol) were treated according to the procedure¹³ described for the corresponding *S*-stereoisomer. The crude product (440 mg, 95.5%) was crystallized from light petroleum and recrystallized from methanol. Yield 320 mg (69.5%), m.p. 139–141 °C; ref.¹³ 139–140 °C. ^1H NMR spectrum in accord with data in ref.¹³. $[\alpha]_{589} 16.7$, $[\alpha]_{546} 21.9$ (25 °C, c 0.71, CHCl_3); ref.¹³ for the *S*-compound $[\alpha]_{589} -16.8$, $[\alpha]_{546} -22.0$.

Single Crystal X-Ray Diffraction

Compound 2a: $\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}_4 \cdot 0.5\text{H}_2\text{O}$, $M = 335.32$, orthorhombic, space group $Pna2_1$ (No. 33), $a = 13.485(2)$, $b = 20.054(2)$, $c = 11.678(2)$ Å, $V = 3158.1(8)$ Å³, $F(000) = 1$ 400, $D_c = 1.411$ g cm^{-3} , $Z = 8$. A colourless plate of the dimensions $0.24 \times 0.3 \times 0.04$ mm (grown from water) was measured at 150 K on a CAD4 diffractometer with $\text{MoK}\alpha$ radiation, $\lambda = 0.71073$ Å. Three standard reflections monitored every 1 h displayed a 2.6% intensity decrease. From a total of 2 836 reflections measured by the θ - 2θ scan in the range $h = 0$ to 15,

$k = 0$ to 22, $l = -13$ to 0, 2 621 were independent and 2 025 of them were regarded as observed according to the $I > 2\sigma(I)$ criterion. Absorption was neglected ($\mu = 0.106 \text{ mm}^{-1}$). The structure was solved by direct methods (SHELXS86)¹⁸ and refined by full-matrix least squares based on F^2 (SHELXL93)¹⁹. The N- and O-bonded hydrogen atoms were refined isotropically except for those at N22, O1 and O2 which behave erratically in refinement and were therefore fixed in positions found from the difference map. The aromatic hydrogens were fixed in calculated positions. The restrained hydrogen atoms were assigned temperature parameters of 1.2 multiples of those of their bonding partners. Hydration was found to be disordered over two positions, the relative population of which was fixed at 0.7 : 0.3 at the final stage of refinement. The model converged to $R = 0.0417$, $wR = 0.1024$, GOF = 1.169 for 507 parameters, maximal residual electron density being 0.45, $-0.26 \text{ e } \text{Å}^{-3}$.

Compound 2b: $\text{C}_{24}\text{H}_{30}\text{N}_4\text{O}_4 \cdot 3\text{H}_2\text{O}$, $M = 492.56$, monoclinic, space group $C2/c$ (No. 15), $a = 7.7090(8)$, $b = 19.741(3)$, $c = 17.172(3) \text{ Å}$, $\beta = 98.28(1)^\circ$, $V = 2 586.1(7) \text{ Å}^3$, $F(000) = 1 056$, $D_c = 1.265 \text{ g cm}^{-3}$, $Z = 4$. A colourless plate of the dimensions $0.2 \times 0.6 \times 0.7 \text{ mm}$ (grown from water) was measured at 150 K on a CAD4 diffractometer with $\text{MoK}\alpha$ radiation, $\lambda = 0.71073 \text{ Å}$. Three standard reflections monitored every 1 h displayed 6% intensity decrease. From a total of 2 581 reflections measured by the θ -2 θ scan (learn-profile) in the range $h = 0$ to 9, $k = 0$ to 23, $l = -20$ to 20, 2 282 were independent ($R_{\text{int}} = 0.012$) and 1 813 of them being regarded as observed according to the $I > 2\sigma(I)$ criterion. Absorption was neglected ($\mu = 0.093 \text{ mm}^{-1}$). The structure was solved by direct methods (SHELXS86)¹⁸ and refined by full-matrix least squares based on F^2 (SHELXL93)¹⁹. Hydrogen atoms were refined isotropically and assigned temperature parameters of 1.2 multiples of those of their bonding partners. The refinement converged to $R = 0.0363$, $wR = 0.0909$, GOF = 1.035 for 231 parameters, maximal residual electron density being 0.28, $-0.19 \text{ e } \text{Å}^{-3}$.

Compound 2c: $\text{C}_{48}\text{H}_{46}\text{N}_4\text{O}_4 \cdot \text{CH}_3\text{OH}$, $M = 774.92$, hexagonal, space group $P6_522$ (No. 179), $a = 13.485(3)$, $c = 40.263(7) \text{ Å}$, $V = 6 341(2) \text{ Å}^3$, $F(000) = 2 472$, $D_c = 1.218 \text{ g cm}^{-3}$, $Z = 6$. A colourless parallelepiped of the dimensions $0.7 \times 0.7 \times 0.9 \text{ mm}$ (grown from methanol) was measured at 170 K on a CAD4 diffractometer with $\text{MoK}\alpha$ radiation, $\lambda = 0.71073 \text{ Å}$. From 2 271 reflections measured by the θ -2 θ scan in the range $h = 0$ to 13, $k = 0$ to 8, $l = 0$ to 47, 1 965 were regarded as observed according to the $I > 2\sigma(I)$ criterion. Absorption was neglected ($\mu = 0.079 \text{ mm}^{-1}$). The structure was solved by direct methods (SHELXS86)¹⁸ and refined in P_522 group by full-matrix least squares based on F^2 (SHELXL93)¹⁹. The aromatic and methyl hydrogens were fixed in calculated positions, the amide and tertiary hydrogens were refined isotropically and assigned temperature parameters of 1.2 multiples of those of their bonding partners. The methanol molecule is disordered and was modelled as two 50 : 50 positions related by a two-fold axis; methanol hydrogens were not found. The correction for secondary extinction with the refined coefficient of 0.0063(22) was applied. The final values are $R = 0.0491$, $wR = 0.1370$, GOF = 1.032 for 280 parameters, maximal residual electron density being $0.55 \text{ e } \text{Å}^{-3}$ around the disordered methanol.

Crystallographic data for the structures **2a–2c** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-162873 (**2a**), CCDC-162874 (**2b**) and CCDC-162875 (**2c**). Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk. and are also available from the author (I.C.) in the form of standard CIF files as produced by SHELX.

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