

Graph-set and packing analysis of hydrogen-bonded networks in polyamide structures in the Cambridge Structural Database

W. D. Samuel Motherwell,*
Gregory P. Shields and Frank H.
Allen

Cambridge Crystallographic Data Centre, 12
Union Road, Cambridge CB2 1EZ, England

Correspondence e-mail:
motherwell@ccdc.cam.ac.uk

Received 25 February 2000

Accepted 11 May 2000

The hydrogen-bond networks and crystal packing of 81 unique secondary di- and polyamides in the Cambridge Structural Database are investigated. Graph-set analysis, as implemented in the *RPluto* program, is used to classify network motifs. These have been rationalized in terms of the relative dispositions of the amide groups. Peptide and retropeptides exhibit significant conformational flexibility, which permits alternative hydrogen-bonding patterns. In peptides, dihedral angles of $-\psi \simeq \varphi \simeq 105^\circ$ allow an antiparallel ladder arrangement, containing rings of either the same or alternating sizes. For retropeptides, and diamides with an odd number of CH_2 spacers, this conformation leads to a parallel ladder with rings of equal size. If φ approaches -60° and ψ 180° , ladders adopt a helical twist, and if the conformation is distorted further, a three-dimensional network is usually adopted. Diamides with aromatic or an even number of CH_2 spacers generally form either antiparallel ladders or sheets, although some exhibit both polymorphs. Symmetry relationships within and between hydrogen-bonded chains, ladders and sheets in the crystal packing have also been analysed. Polyamides form considerably more complex networks, although many of the structural motifs present in the diamides occur as components of these networks.

1. Introduction

It is well established that the strong hydrogen bonds found in organic systems have a profound influence on the crystal structures adopted by compounds with N/O—H donor and/or O/N acceptor functional groups (Jeffrey, 1997). An understanding of the motifs and networks mediated by these interactions is essential to many fields of research, *e.g.* supramolecular synthesis (Nangia & Desiraju, 1998), crystal engineering (Etter, 1991; Aakeroy & Seddon, 1993; Aakeroy, 1997; Desiraju, 1995, 1997), *ab initio* crystal structure prediction (Price & Wibley, 1997; Motherwell, 1999; Mooij *et al.*, 1998) and the modelling of protein–ligand interactions in biological systems (Jeffrey & Saenger, 1991; Bruno *et al.*, 1997; Verdonk *et al.*, 1999). A number of early studies explored the nature of hydrogen-bonded motifs and networks formed by compounds with particular functional groups, *e.g.* carbohydrates (Jeffrey & Takagi, 1978), carboxylic acids (Leiserowitz & Schmidt, 1969) and amides (Leiserowitz, 1976; Leiserowitz & Tuval, 1978).

In order to describe hydrogen-bonded motifs and networks systematically, a graph-set approach was suggested by Kuleshova & Zorkii (1980; Zorkii & Kuleshova, 1980) and later developed by Etter (1990), Etter *et al.* (1990) and Bernstein *et al.* (1995). This provides a description of hydrogen-bonding

patterns in terms of chains (**C**), rings (**R**), discrete complexes (**D**) and intramolecular (self-associating) rings (**S**). The degree of the pattern (n , the number of atoms comprising the pattern; in the case of chains **C** this is the pattern repeat unit), together with the numbers of donors (d) and acceptors (a), are combined to form the quantitative graph set descriptor $\mathbf{X}_d^a(n)$. For convenience, the alternative notation $\mathbf{X}a,d(n)$ has been adopted in this paper. More recently, the graph-set approach has been placed on a more rigorous graph-theoretical footing (Grell *et al.*, 1999). This introduced a number of new concepts. In particular, network paths are described by a directed label sequence, e.g. a hydrogen-bond path $\overrightarrow{a} \overrightarrow{a} \overrightarrow{b} \overleftarrow{a} \overleftarrow{a} \overleftarrow{b}$ where the labels a and b represent *types* of crystallographically independent hydrogen bond ('H-edges'), and the arrow indicates the hydrogen-bond direction (\rightarrow donor–acceptor, \leftarrow acceptor–donor). The *qualitative* graph-set descriptor $\mathbf{G}(\overrightarrow{a} \overrightarrow{a} \overrightarrow{b} \overleftarrow{a} \overleftarrow{a} \overleftarrow{b})$ describes the type of hydrogen-bond pattern defined by this hydrogen-bond path (**C**, **R**, **D** or **S**). Patterns are distinguished on the basis of their *level*, the first level comprising graph sets for paths involving one type of hydrogen bond and the second level involving two types *etc.* It is convenient to summarize the first- and second-levels in matrix form with the first-level motifs on the leading diagonal and the second-level patterns as the off-diagonal terms.

These topological descriptors had already proved useful in decoding the differences between packing networks in polymorphic systems (e.g. Bernstein, 1991; Bernstein *et al.*, 1990; Bernstein *et al.*, 1995; Aakeroy *et al.*, 1998) and in particular classes of compounds, e.g. phenol–amine networks (Coupar *et al.*, 1997; Ferguson, Bell *et al.*, 1997; Ferguson, Coupar & Glidewell, 1997; Ferguson *et al.*, 1998b; Ferguson, Glidewell, Gregson, Meehan & Patterson, 1998), phenylphosphonic acid adducts (Ferguson *et al.*, 1998a), alcohol–amine co-crystals (Loehlin *et al.*, 1998) and 1,4-dihydro-2,3-quinoxalinediones (Kubicki *et al.*, 1996). Recently, algorithms have been developed for automatic graph-set assignment, up to second level (Motherwell *et al.*, 1999, 2000), which enable graph-set analyses to be performed routinely.

The structures of secondary (*i.e.* without terminal NH_2 groups) di- and polyamides have been determined for a variety of reasons, but principally because they model the peptide chains of biological systems (Pauling *et al.*, 1951; Pauling & Corey, 1951, 1953) or the synthetic polyamide polymers, e.g. nylon-6,6 and 6,10 (Bunn & Garner, 1947), nylon-4,4 (Fredericks *et al.*, 1966), nylon-7,7 (Kinoshita, 1959) and those with aromatic (e.g. Northolt, 1974) or mixed aromatic/aliphatic (e.g. Ota *et al.*, 1966) spacers, the crystal structures of which have themselves been determined. As a result, the diamides fall into three distinct classes: peptides or retropeptides, which have a single CR_n group separating the amide groups, diamides with straight-chain aliphatic spacers and those with aromatic spacer groups, the latter two types being related to synthetic polymers.

In this paper, the Cambridge Structural Database (CSD; Allen & Kennard, 1993) is used to detect and classify the hydrogen-bonded networks formed by di- and polyamides with the aid of graph-set analysis and the secondary structures,

i.e. the manner in which the hydrogen-bonded chains, ladders or sheets are themselves arranged in the crystal structure, are compared and analysed. The recurring motifs are related to the known structural features of polypeptides and synthetic polyamides.

2. Methodology

2.1. Data retrieval

A *Quest3D* search of the CSD (April 1999 release, 197 481 entries) was made for structures containing two or more amide groups $\text{C}(=\text{O})-\text{N}(\text{H})$ with no cyclic routes to atoms outside the amide fragments, no elements other than C, H, N and O present, and atomic coordinates stored. Structures with terminal NH_2 groups or additional N and O atoms not in $\text{X}-\text{C}(=\text{O})-\text{N}(\text{H})-\text{X}$ functional groups (where $\text{X} = \text{C}, \text{H}$) were excluded. Structures containing solvent molecules other than hydrocarbons were rejected, resulting in a subset of 88 structures.¹ Initially, seven duplicate structure determinations were retained, in order to analyse whether these represented the same or different polymorphs. However, in all cases the analysis revealed that all these were repeat determinations of the same crystal structure and the duplicates were not analysed further.

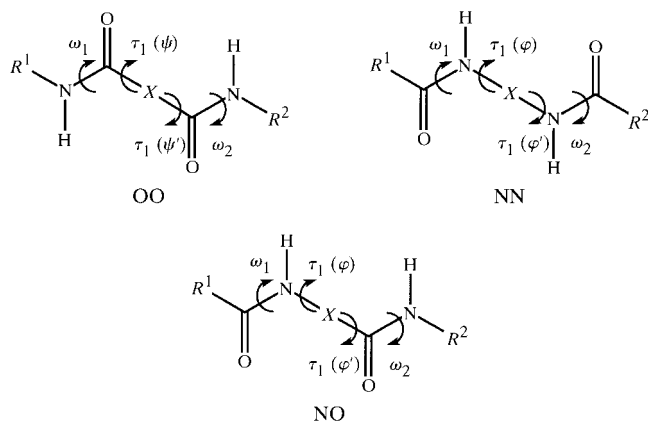
2.2. Data analysis

The hydrogen-bond networks and packing arrangements were analysed, graph-set analysis performed and figures generated using *RPluto*, the research version of the CSD *PLUTO* program² with features for automatic hydrogen-bond assignment. In the figures, the symmetry-equivalent hydrogen bonds are shown in the same colour and where appropriate the first-level graph sets are shown in the same colour as the respective hydrogen bonds and second-level graph sets in a different colour. For structures without amide H atoms present, these were added in geometrically idealized positions using the HCAL function in *PLUTO*. Otherwise, existing H-atom coordinates were normalized to values obtained from neutron diffraction studies, unless the coordinates were clearly in error, in which case they were replaced with idealized H positions. Intramolecular geometric data were generated automatically in *Quest3D* sub-searches for structures whose coordinates were matched with the chemical connectivity representation, otherwise the parameters were derived in *PLUTO*. The geometric parameters used in this study are defined in (I) for amide groups separated by a single spacer atom X (the torsion angles τ are conventionally labelled as φ and ψ in peptide structures). In addition, dihedral angles τ between the mean planes through the amide, spacer and terminal groups, and the angle between the $\text{C}=\text{O}$ vectors $\theta(\text{CO}, \text{CO})$, were calculated. The chemical constitutions of the

¹ Supplementary data for this paper, including CSD refcodes and references for these structures, are available from the IUCr electronic archives (Reference: BM0028). Services for accessing these data are described at the back of the journal.

² This program for UNIX platforms is available freely for academic research use from the CCDC website <http://www.ccdc.cam.ac.uk/prods/rpluto>.

amides and the values of these parameters are given in Tables 1–4.



3. Results and discussion

3.1. Diamides

Diamides may be divided into three classes – **OO** retropeptides (16 examples), **NN** retropeptides (24) and **ON** peptides (21) – depending on the relative positions of the C=O and N–H groups on the organic backbone [(I) shows these diamide types where the amide groups are separated by one C atom]. The architectures can be classified into finite complexes, chains and ladders one-dimensional, two-dimensional sheets and three-dimensional networks, depending on how the hydrogen bonds propagate through the structure. The manner in which these supramolecular architectures are arranged to form the three-dimensional crystal can be considered as higher-order (*i.e.* secondary and tertiary) aspects of the structure. Leiserowitz & Tuval (1978) discussed the available structures of **OO** and **NN** types, which formed ladders by translation or sheets *via* a glide plane or 2_1 axis. Graph sets and intramolecular conformations are detailed in Tables 1–3 for diamides with CR_n , $[CH_2]_n$ and aromatic spacer groups, respectively.³

In the text, the degree n of the graph sets is generally expressed in terms of the number of atoms l separating the amide groups, to show the relationships between graph sets for similar compounds with different l more clearly. However, the numeric values for n are given in Tables 1–3.

3.1.1. Finite complexes. POLPEL ($R^1 = \text{Ph}$) is closely related to POLNIN ($R^1 = \text{Me}$), but the central donor and acceptor do not form any **R**2,2(10) rings as does the latter (see below), and the other donor and acceptor form a hydrogen-bonded **R**6,6(36 + 6*l*) ring (where $l = 1$ is the length of the carbon chain separating the amide groups) about a threefold inversion axis rather than **C** $n,n(n\{6 + l\})$ chains as in JUDZEN and POLPEL.

3.1.2. Chain structures. In a few instances, diamides form a strong intramolecular hydrogen bond and thus there is only

one donor and one acceptor available for intermolecular hydrogen bonding. LABJED ($l = 4$, **NN**) forms an **S**(5 + l) intramolecular ring with a 2.10 Å H···O distance [$N\cdots O = 2.814(5)$ Å], in addition to a **C**(5 + l) chain of molecules related by translation. Similarly, VEHNUR ($l = 3$, **NN**) forms an **S**(5 + l) ring (H···O 1.92 Å) and also forms a **C**1,1(5 + l) chain, molecules being related by a glide rather than translation. POLPIP has quite a different conformation to its analogues POLPEL and POLNIN [φ and ψ *gauche* (*G*) rather than antiperiplanar (*A*), Table 1], giving an intramolecular N–H···N(H)(C=O) contact of 2.28 Å: the other N–H group forms a simple **C**1,1(4) chain.

3.1.3. Ladder structures. Two dimensional ladder structures can be divided into two principal classes: those in which the hydrogen bonds run parallel (shown schematically in Fig. 1*a*) or antiparallel (Fig. 1*b*). These networks have been variously termed ‘belts’ (Shintani, 1960; Harada & Iitaka, 1977), ‘ribbons’ (Brisson & Brisse, 1982) or ‘ladder-like ribbons’ (Pineault & Brisse, 1983*a,b*). Whether the parallel or antiparallel arrangement is more favourable is related to the class of diamide and the nature of the carbon backbone separating the amide groups, since these factors affect the geometry of the N–H···O=C interaction (Wells, 1954). The N–H···O angle of this hydrogen bond is closely linear for all-antiperiplanar aliphatic chains when the hydrogen bonds are parallel for **OO** and **NN**, and antiparallel for **NO**.

Two alternative parallel ladder (Fig. 1*a*) arrangements are possible where the two amide functions are crystallographically independent. These differ in whether each amide function forms a hydrogen bond with a symmetry-related copy of itself (forming a consecutive ladder) or of the other, crystallographically independent, amide group (forming an alter-

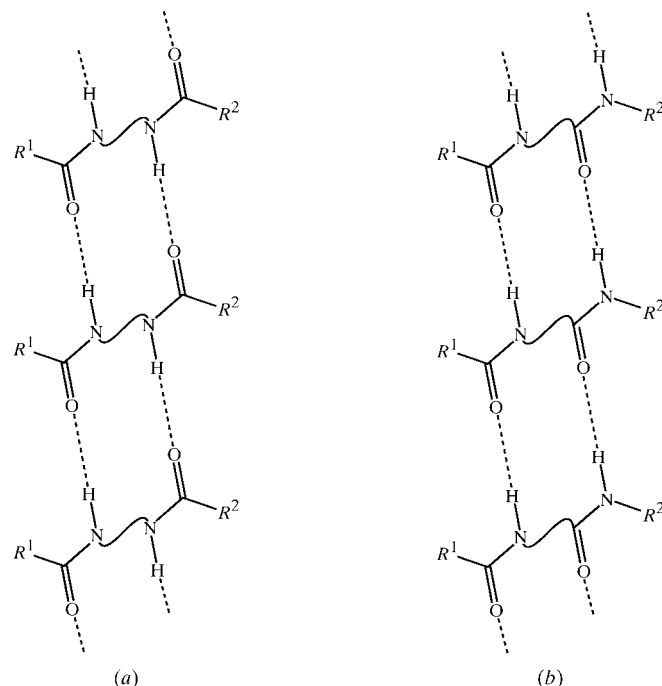


Figure 1
(*a*) Parallel and (*b*) antiparallel hydrogen-bonded ladder arrangements.

³ Additional example figures for some of the diamide structures have also been deposited as supplementary material (see footnote 1).

Table 1

Diamides linked by methylene chains.

Point group: crystallographic point symmetry of molecule(s). $-\text{[CH}_2\text{]}_n-$ conformation: torsion angles around C–C bonds: *A* = antiperiplanar (150 to 180° and –150 to –180°), *+G gauche* (30 to 90°), *–G = gauche* (–30 to –90°).

<i>n</i>	Refcode	Point group	Graph set	R^1, R^2	$\tau(R^1, R^2)$ (°)	$\tau(R, \text{NCO})$ (°)	$\tau(R, \text{[CH}_2\text{]}_n)$ (°)	$\tau(\text{NCO}, \text{[CH}_2\text{]}_n)$ (°)	$\tau(\text{NCO}, \text{NCO})$ (°)	$\theta(\text{CO}, \text{CO})$ (°)	$-\text{[CH}_2\text{]}_n-$ conformation	Network
(i) $R^1\text{C(=O)NH(CH}_2\text{)}_n\text{NHC(=O)R}^2$ NN												
0	FOMHAZ	C_i	$\text{C1,1(4), C1,1(5)}\vec{a}$, $\text{C2,2(10)}\vec{a}\vec{a}$	H, H	–	–	–	–	0	180	–	Puckered sheet
0	DIACHZ	C_{2h}	$\text{C1,1(4), R2,2(10)}\vec{a}$, $\text{C2,2(10)}\vec{a}\vec{a}$	Me, Me	–	–	–	–	0	180	–	Antiparallel ladder
2	ETBZAM	C_i	$\text{C1,1(4), C1,1(7)}\vec{a}$, $\text{C2,2(14)}\vec{a}\vec{a}$	Ph, Ph	0	18.9	69.5	88.3	0	180	<i>A</i>	Puckered sheet
4	MEBZAM	C_i	$\text{C1,1(4), R2,2(18)}\vec{a}$, $\text{C2,2(18)}\vec{a}\vec{a}$	Ph, Ph	0	29.7	19.6	10.1	0	180	<i>AAA</i>	Antiparallel ladder
4	SAZWEV	C_i	$\text{C1,1(4), C1,1(9)}\vec{a}$, $\text{C2,2(18)}\vec{a}\vec{a}$	^t BuC ₆ H ₄ , ^t BuC ₆ H ₄	0	27.2	52.6	79.8	0	180	<i>AAA</i>	Puckered sheet
4	TOPPUJ	C_i	$\text{C1,1(4), R2,2(18)}\vec{a}$, $\text{C2,2(18)}\vec{a}\vec{a}$	H, H	–	–	–	5.1	0	180	<i>AAA</i>	Antiparallel ladder
6	BAGJAU10	C_i	$\text{C1,1(4), R2,2(22)}\vec{a}$, $\text{C2,2(22)}\vec{a}\vec{a}$	Ph, Ph	0	29.1	20.5	8.8	0	180	<i>AAAAA</i>	Antiparallel ladder
6	TOPQAO	C_i	$\text{C1,1(4), R2,2(22)}\vec{a}$, $\text{C2,2(22)}\vec{a}\vec{a}$	H, H	–	–	–	0.8	0	180	<i>AAAAA</i>	Antiparallel ladder
6	DAMEDA	C_i	$\text{C1,1(4), R2,2(22)}\vec{a}$, $\text{C2,2(22)}\vec{a}\vec{a}$	Me, Me	–	–	–	11.6	0	180	<i>AAAAA</i>	Antiparallel ladder
6	HEXMPR	C_i	$\text{C1,1(4), R2,2(22)}\vec{a}$, $\text{C2,2(22)}\vec{a}\vec{a}$	Et, Et	–	–	–	11.1	0	180	<i>AAAAA</i>	Antiparallel ladder
7	BIWROO	C_1	$\text{C1,1(4)}\vec{a}$, $\text{C1,1(4)}\vec{b}$, $\text{C2,2(24)}\vec{a}\vec{b}$, $\text{R2,2(24)}\vec{a}\vec{b}$	Ph, Ph	78.2	28.4, 34.8	62.8, 45.4	89.6, 79.3	51.0	43.0	<i>AAAAAA</i>	Parallel ladder
8	CACHIX	C_i	$\text{C1,1(4), R2,2(26)}\vec{a}$, $\text{C2,2(26)}\vec{a}\vec{a}$	Ph, Ph	0	29.1	20.5	9.1	0	180	<i>AAAAAAA</i>	Antiparallel ladder
8	TOPQEU	C_i	$\text{C1,1(4), R2,2(26)}\vec{a}$, $\text{C2,2(26)}\vec{a}\vec{a}$	H, H	–	–	–	6.8	0	180	<i>AAAAAAA</i>	Antiparallel ladder
(ii) $R^1\text{NHC(=O)(CH}_2\text{)}_n\text{C(=O)NHR}^2$ OO												
	DMOXAM	C_i	$\text{C1,1(4), R2,2(10)}\vec{a}$, $\text{C2,2(10)}\vec{a}\vec{a}$	Me, Me	–	–	–	–	0	180	–	Antiparallel ladder
3	ZALVEN	C_2	$\text{C1,1(4), R2,2(16)}\vec{a}$, $\text{C2,2(16)}\vec{a}\vec{a}$	ⁿ Pr, ⁿ Pr	–	–	–	78.9	82.8	149.4	<i>+G+G</i>	Antiparallel ladder
4	BOXFAV	C_i	$\text{C1,1(4), C1,1(9)}\vec{a}$, $\text{C2,2(18)}\vec{a}\vec{a}$	Ph, Ph	0	27.9	12.3	39.7	0	180	<i>AAA</i>	Puckered sheet
4	ETADAM10	C_i	$\text{C1,1(4), R2,2(18)}\vec{a}$, $\text{C2,2(18)}\vec{a}\vec{a}$	Et, Et	0	–	–	86.5	0	180	<i>+GA–G</i>	Antiparallel ladder

nating ladder): both have the qualitative graph set $\text{C}(\vec{a})$, $\text{C}(\vec{b})$, $\text{C}(\vec{a}\vec{b})$, $\text{R}(\vec{a}\vec{b})$. The first type is represented by BIWROO ($l = 7$, **NN**, Fig. 2a): $\text{C1,1(4)}\ \text{C1,1(4)}$, $\text{C2,2(2[5 + }l\text{])}$, $\text{R2,2(2[5 + }l\text{])}$, successive molecules being related by a translation along **a**, and the latter by JOFHOB ($l = 1$, **OO**, Fig. 2b): $\text{C1,1(5 + }l\text{)}$, $\text{C1,1(5 + }l\text{)}$, C2,2(8) , $\text{R2,2([4 + }l\text{][6 + }l\text{])}$, molecules being related by a 2_1 screw axis along **b**, allowing the terminal hydrophobic ^tBu and central ⁿPr groups to interlock along the zigzag ribbon. If the diamide lies on a mirror plane, as in JOFHER ($l = 1$, **NN**) and HEYREI ($l = 1$, **OO**), there is only one crystallographically independent hydrogen bond with first-level graph set $\text{C1,1(4)}\ \text{C1,1(5 + }l\text{)}$ $\text{R2,2(2[5 + }l\text{])}$. JOFHER and HEYREI differ in that adjacent molecules in the ladder are related in JOFHER by translation (*Pbcm*) and by a glide plane in HEYREI (*Cmc2₁*), which allows ^tBu and Ph groups to interlock in the latter, as in JOFHOB. The conformations of JOFHER, HEYREI and JOFHOB are similar, with $\psi \simeq -\psi'$ (or $\varphi \simeq -\varphi'$) $\simeq 100$ – 110° (relationship is exact for molecules lying on a mirror). TIRJIN ($l = 1$, **NO**) forms a similar network, but has two crystallographically independent

molecules in the asymmetric unit (enantiomers which also differ in the conformation of the Et group), which alternate along the **DDDD** $2[\text{C2,2(8)}]\ 2[\text{C2,2(2[5 + }l\text{])}]\ 2[\text{R2,2(2[5 + }l\text{])}]$ ladder.

The antiparallel ladder arrangement (Fig. 1b) is rather more common, particularly because of the large number of diamides **OO** and **NN** with C_i symmetry which form ladders. As with the parallel chains, there are two principal arrangements, in which equivalent hydrogen bonds are consecutive [qualitative graph set $\text{C}(\vec{a})$, $\text{C}(\vec{b})$, $\text{R}(\vec{a}\vec{b})$, $\text{C}(\vec{a}\vec{b})$] or alternate [$\text{R}(\vec{a})_2$ $\text{R}(\vec{b})_2$ $\text{C}(\vec{a}\vec{b})$ $\text{C}(\vec{a}\vec{b})$]. These two arrangements for polypeptides **NO** with $l = 1$ are known respectively in biochemistry as the parallel chain pleated sheet (PCP) and antiparallel chain pleated sheet (ACP) β -sheet structures (Pauling & Corey, 1951, 1953), and differ in whether the rings are of the same or alternating sizes [the terms parallel and antiparallel refer to the directions of the peptide chains, not the hydrogen bonds]. In the former, molecules are typically related by translation, e.g. diamides **NO** APALAM ($l = 1$, Fig. 3a) and APHAMA ($l = 1$) with a $\text{C1,1(4)}\ \text{C1,1(4)}\ \text{C2,2(2[}l + 5\text{])}$

Table 2

Diamides linked by aromatic or other spacer groups.

Point group: crystallographic point symmetry of molecule(s).

Refcode	Point group	Graph set	<i>X</i>	<i>R</i> ¹ , <i>R</i> ²	$\tau(R^1, R^2)$ (°)	$\tau(R, NCO)$ (°)	$\tau(R, X)$ (°)	$\tau(NCO, X)$ (°)	$\tau(NCO, NCO)$ (°)	$\theta(CO, CO)$ (°)	$\tau(X, X)$ (°)	Network
(i) <i>R</i> ¹ C(=O)NH– <i>X</i> –NHC(=O) <i>R</i> ² NN												
BZOPDA10	<i>C</i> _i	C1,1(4), C1,1(9)<i>a</i> C2,2(18)<i>a</i>	1,4-C ₆ H ₄	Ph, Ph	0	24.7	79.4	54.9	0	180	–	Puckered sheet
PABZAM	<i>C</i> _i	C1,1(4), R2,2(18)<i>a</i> C2,2(18)<i>a</i>	1,4-C ₆ H ₄	Ph, Ph	0	29.4	64.5	35.5	0	180	–	Antiparallel ladder
TERSEO	<i>C</i> _i	C1,1(4), R2,2(18)<i>a</i> C2,2(18)<i>a</i>	1,4-C ₆ H ₄	<i>p</i> Tol, <i>p</i> Tol	0	28.7	58.0	30.0	0	180	–	Antiparallel ladder
LABJED	<i>C</i> _i	C1,1(9)<i>a</i> S1,1(9)<i>b</i>	2,2'-C ₆ H ₄ - C ₆ H ₄	Me, Me	–	–	–	32.5, 76.7	82.4	71.8	89.3	Chain
FAPFAD	<i>C</i> _i	C1,1(4), R2,2(30)<i>a</i> C2,2(30)<i>a</i>	3,3'-C ₆ H ₄ - C ₄ -C ₆ H ₄	Me, Me	–	–	–	44.7	0	180	0	Antiparallel ladder
HIDDUT†		C1,1(4), R2,2(18)<i>a</i>	C ₆ H ₄	C ₆ H ₄ , C ₆ H ₄	–	30.0	67.8	38.0	0	180	–	Polymeric sheet
VEHNUR	<i>C</i> ₁	C1,1(8)<i>a</i> S1,1(8)<i>b</i>	CH=C(Me)- C(H)Et	Ph, Ph	78.4	41.8, 14.8	–	–	44.7	77.7	–	Chain
(ii) <i>R</i> ¹ NHC(=O)– <i>X</i> –C(=O)NHR ² OO												
DPTPAM	<i>C</i> _i	C1,1(4), R2,2(18)<i>a</i> C2,2(18)<i>a</i>	C ₆ H ₄	Ph, Ph	0	30.0	60.7	31.0	0	180	–	Antiparallel ladder
HIDDUT†		C1,1(4), R2,2(18)<i>a</i>	C ₆ H ₄	C ₆ H ₄ , C ₆ H ₄	–	38.0	67.8	30.0	0	180	–	Polymeric sheet
RAPYUC	<i>C</i> ₁	C1,1(9)<i>a, b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(18)<i>a</i> <i>a</i> <i>b</i>	1,4-C ₁₀ H ₆	Me, Me	–	–	–	52.0, 65.6	15.1	59.5	–	Sheet
PULHUZ	<i>C</i> ₁	D1,1(2)<i>a, b, c, d</i> <i>a</i> <i>b</i> <i>c</i> <i>d</i> C2,2(8)<i>a</i> <i>a</i> <i>d</i> <i>b</i> <i>c</i> C2,2(16)<i>a</i> <i>a</i> <i>b</i> <i>c</i> <i>d</i> R2,2(16)<i>a</i> <i>a</i> <i>c</i> <i>b</i> <i>d</i>	1,3-C ₆ H ₄	Ph, Ph	4.3	34.4, 29.1	6.5, 6.5	30.7, 30.5	54.7	131.8	–	Antiparallel ladder
RAPYIQ	<i>C</i> _i	C1,1(4), R2,2(22)<i>a</i> C2,2(22)<i>a</i>	1,4-CH ₂ - C ₄ H ₆ -CH ₂	Me, Me	–	–	–	75.6	–	180	–	Antiparallel ladder
RAPYOW	<i>C</i> _i	C1,1(4), C1,1(11)<i>a</i> C2,2(22)<i>a</i>	2,6-C ₁₀ H ₆	Me, Me	–	–	–	25.8	–	180	–	Antiparallel ladder
ZUKJUK	<i>C</i> ₁	R2,2(26)<i>a, b</i> <i>a</i> <i>b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(26)<i>a</i> <i>a</i> <i>b</i>	4,4'-C ₆ H ₄ - C ₆ H ₄	Me, Me	–	–	–	45.3, 22.7	13.1	166.6	35.3	Antiparallel ladder
ZUKKAR	<i>C</i> _i	D1,1(2)<i>a, b</i> <i>a</i> <i>b</i> C2,2(30)<i>a</i> <i>a</i> <i>b</i>	4,4'-C ₆ H ₄ - (C ₂)-C ₆ H ₄	Me, Me	–	–	–	11.2	0	180	0	Antiparallel ladder
Molecule A	<i>C</i> _i	C2,2(8) [R2,2(30)] [R4,4(38)]<i>a</i> <i>b</i>						48.8	0	180	0	
Molecule B	<i>C</i> _i											
ZUKJOE	<i>C</i> ₁	R2,2(30)<i>a, b</i> <i>a</i> <i>b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(30)<i>a</i> <i>a</i> <i>b</i>	4,4'-C ₆ H ₄ - (<i>z</i> -C ₂ H ₂)- C ₆ H ₄	Me, Me	–	–	–	39.6, 27.0	15.9	164.2	28.1	Antiparallel ladder
YEKCIA	<i>C</i> ₁	R2,2(16)<i>a, b</i> C1,1(8)<i>b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(16)<i>a</i> <i>a</i> <i>b</i>	CH(CH ₂ CH=CH ₂)- CH ₂ CH(CH ₂ cy- C ₆ H ₁₁)	CHMe- Ph, CH- MePh	–	–	–	–	53.3	108.2	–	3d network
(iii) <i>R</i> ¹ C(=O)NH– <i>X</i> –C(=O)NHR ² NO												
JEPHIV	<i>C</i> ₁	R2,2(18)<i>a, b</i> R2,2(22)<i>b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(20)<i>a</i> <i>a</i> <i>b</i>	1-CH ₂ ,7-C ₁₀ H ₆	Me, ^{<i>i</i>} Pr	–	–	–	–	62.4	115.2	–	Antiparallel ladder
JEPHOP	<i>C</i> ₁	D1,1(2) <i>a, c</i> R2,2(16) <i>b, d</i> <i>a</i> <i>c</i> R2,2(20)<i>a</i> <i>a</i> <i>c</i>	1-CH ₂ ,7-bicyclo- CH(CH ₂) ₃ CCHC(CH) ₂ C	Me, ^{<i>i</i>} Pr	–	–	–	–	89.3	129.8	–	Antiparallel ladder
Molecule A									81.9	126.9		
Molecule B												
NAKLOA	<i>C</i> ₁	C1,1(7)<i>a, b</i> C1,1(9)<i>b</i> C2,2(8)<i>a</i> <i>a</i> <i>b</i> C2,2(16)<i>a</i> <i>a</i> <i>b</i>	1,3-cy-C(H) CMe ₂ CHCH ₂	Me, ^{<i>i</i>} Pr	–	–	–	–	25.1	167.2	–	3d network

† Polymer –[C(O)N(H)–C₆H₄–N(H)C(O)–C₆H₄]– comprising adjacent **NN** and **OO** units.

R2,2($\{l + 4\}\{l + 6\}$) ladder pattern. Since *l* is odd, the diamide groups are not quite antiparallel (typically the angle between the C–O vectors being 150–160°, Table 1) and $\psi \simeq -\varphi$. ALEUIP (**NO**, *l* = 1) has the same graph set, but the ladders have a helical twist, adjacent molecules along the ladder being related by a 4₁ screw axis. As a consequence, the conformation

is twisted relative to APALAM and APHAMA, φ being closer to –G and ψ to A.

Diamides **OO** VISFEI (*l* = 1), ZUKJOE (*l* = 10) and ZUKJUK (*l* = 8) form ladders of the **R2,2**(2{5 + *l*}) **R2,2**(2{5 + *l*}) **C2,2**(8) **C2,2**({4 + *l*}{6 + *l*}) type, in which adjacent molecules are related by inversion and alternate molecules by

Table 3

Diamides linked by a single carbon atom.

AC = absolute configuration: D = dextrorotatory enantiomer, L = laevorotatory enantiomer, E = unspecified enantiomer, R = racemic

AC	Refcode	Graph set	X	R ¹ , R ²	ω ₁ (°)	τ ₁ (°)	τ ₂ (°)	ω ₂ (°)	τ (NCO, NCO) (°)	θ (C=O, C=O) (°)	Network
(i) R ¹ C(=O)NH-X-C(=O)NHR ² NO						φ	ψ				
E	AGLYPR	C1,1(5)a, C1,1(7)b C2,2(8) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CH ₂	Me, 'Pr	178.3	-78.2	162.4	176.5	87.5	113.9	3d network
R	PIVGLY	R2,2(10)a, R2,2(14)b C2,2(8) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CH ₂	'Bu, 'Pr	-178.7	-112.9	141.1	171.5	56.6	152.0	Antiparallel ladder
L	LAANMA Molecule A Molecule B	D1,1(2)a,b,c,d R2,2(10) $\vec{a} \vec{b}$ C2,2(8) $\vec{a} \vec{c}$, $\vec{b} \vec{d}$ C2,2(12) $\vec{a} \vec{d}$, $\vec{b} \vec{c}$ R2,2(14) $\vec{c} \vec{d}$	CHMe	Me, Me	-168.4	-84.3	159.0	175.3	85.3	126.0	Antiparallel ladder
R	DLANMA		CHMe	Me, Me	-177.7	-75.9	150.1	175.3	86.4	116.9	Disordered Sheet
R	ALNMAM	C1,1(7)a, R2,2(10)b C2,2(8) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CH'Pr	Me, Me	177.2	-93.8	140.4	174.1	72.0	136.5	Disordered Sheet
E	ALEUIP	C1,1(4)a,b R2,2(12) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CH'Pr	Me, 'Pr	-176	-85	156	172	85.6	112.9	Antiparallel ladder
R	APALAM	C1,1(4)a,b R2,2(12) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CHCH ₂ Ph	Me, Me	178.1	-105.5	107.9	-174.9	69.3	156.2	Antiparallel ladder
L	APHAMA	C1,1(4)a,b R2,2(12) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CHCH ₂ Ph	Me, Me	177.7	-106.6	103.7	-176.2	70.4	154.5	Antiparallel ladder
R	NALEUE	C1,1(7)a, R2,2(10)b C2,2(8) $\vec{a} \vec{b}$, $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CHCH ₂ 'Pr	Me, Et	179.0	-89.8	144.1	174.5	75.4	132.2	Sheet
R	NAAIBA	C1,1(5)a, C1,1(7)b C2,2(8) $\vec{a} \vec{b}$ C2,2(12) $\vec{a} \vec{b}$	CMe ₂	Me, Me	-172.7	-55.5	-39.4	-175.0	74.3	37.8	3d network
R	TIRJIN Molecule A Molecule B	D1,1(2)a,b,c,d R2,2(12) $\vec{a} \vec{b}$, $\vec{c} \vec{d}$ C2,2(12) $\vec{a} \vec{d}$, $\vec{b} \vec{c}$ C2,2(8) $\vec{a} \vec{c}$, $\vec{b} \vec{d}$	CEtMe	Me, Me	176.4	57.4	52.3	173.3	85.2	22.2	Parallel ladder
R	POLNIN Molecule A Molecule B	R2,2(10)a, D1,1(2)b,c D3,3(12)a&b, a&c C2,2(14) $\vec{b} \vec{c}$	CPh ₂	Me, Me	-179.3	-163.4	156.1	176.5	25.3	153.6	Puckered tape
R	POLPEL	R6,6(42)a	CPh ₂	Ph, Me	175.9	176.0	-176.3	-177.7	5.4	155.2	Finite ring
R	POLPIP	C1,1(4)a	CPh ₂	Me, CH ₂ Ph	-178.1	-58.3	-33.9	-176.4	72.8	34.0	Chain
R	JUDZEN Molecule A Molecule B	D1,1(2)a,b,c,d R2,2(10) $\vec{a} \vec{c}$ D3,3(12)a&b, a&d, b&c, c&d	C=CH ₂	Me, Me	173.5	-162.6	169.4	179.0	16.4	162.1	Sheet
R	DEBHEX†	C1,1(4)a, b C2,2(12) $\vec{a} \vec{b}$, $\vec{a} \vec{b}$	C=CHPh	Me, Me	177.2	-58.3	148.0	175.4	77.8	105.3	3d network
R	DEBHEX01†	C1,1(4)a, b C2,2(12) $\vec{a} \vec{b}$, $\vec{a} \vec{b}$	C=CHPh	Me, Me	176.4	-56.8	148.7	177.0	76.6	104.8	3d network
(ii) R ¹ C(=O)NH-X-NHC(=O)R ² NN						φ	φ'				
R	JOFHIV Molecule A Molecule B	D1,1(2)a,b,c,d C2,2(8) $\vec{a} \vec{d}$, $\vec{b} \vec{c}$ C2,2(12) $\vec{a} \vec{b}$, $\vec{b} \vec{d}$, $\vec{c} \vec{d}$ R2,2(12) $\vec{a} \vec{c}$	CH ₂	Me, Me	178.0	-93.2	-77.0	178.2	69.1	155.1	3d network
R	EDACTM10	C1,1(4)a,b R4,4(24) $\vec{a} \vec{b}$, $\vec{a} \vec{b}$	CHMe	Me, Me	-176	-80	159	-177	85.0	62.7	Sheet
R	JOFHOB	C1,1(6)a,b C2,2(8) $\vec{a} \vec{b}$ R2,2(12) $\vec{a} \vec{b}$	CH'Pr	'Bu, 'Bu	172	-101	99	-176	75.6	20.6	Parallel ladder
R	HEYREI	C1,1(4)a, C1,1(6)a R2,2(12) $\vec{a} \vec{a}$	CH'Bu	Ph, Ph	165	-105	105	-165	79.8	12.6	Parallel ladder
(iii) R ¹ NHC(=O)-X-C(=O)NHR ² OO						ψ	ψ'				
R	JOFHER	C1,1(4)a, C1,1(6)a R2,2(12) $\vec{a} \vec{a}$	CH'Pr	Me, Me	-179	-110.4	110.4	179	65.2	29.8	Parallel ladder

Table 3 (continued)

AC	Refcode	Graph set	X	R^1, R^2	ω_1 (°)	τ_1 (°)	τ_2 (°)	ω_2 (°)	τ (NCO, NCO) (°)	θ (C=O, C=O) (°)	Network
R	VISFEI	$R2,2(12)a,b$ $C2,2(8)\overrightarrow{a}\overleftarrow{b}$ $C2,2(12)\overrightarrow{a}\overleftarrow{b}$	$C(^nBu)_2$	$1-C_{10}H_7,$ $1-C_{10}H_7$	-172	-58	-55	-171	89.1	13.1	Antiparallel ladder

† These represent different determinations of the same crystal structure.

translation. Where l is even, e.g. ZUKJOE and ZUKJUK, the diamide moieties are aligned approximately antiparallel (Fig. 4a). The secondary structure in these two diamides consists of stacks of ladders (which lie approximately in the {041} plane)

along (001), successive stacks being related by a 2_1 axis along \mathbf{b} (i.e. perpendicular to the stack direction) to give a herringbone tertiary structure. The absence of C_i symmetry in ZUKJUK allows the biphenyl spacer to adopt a non-planar

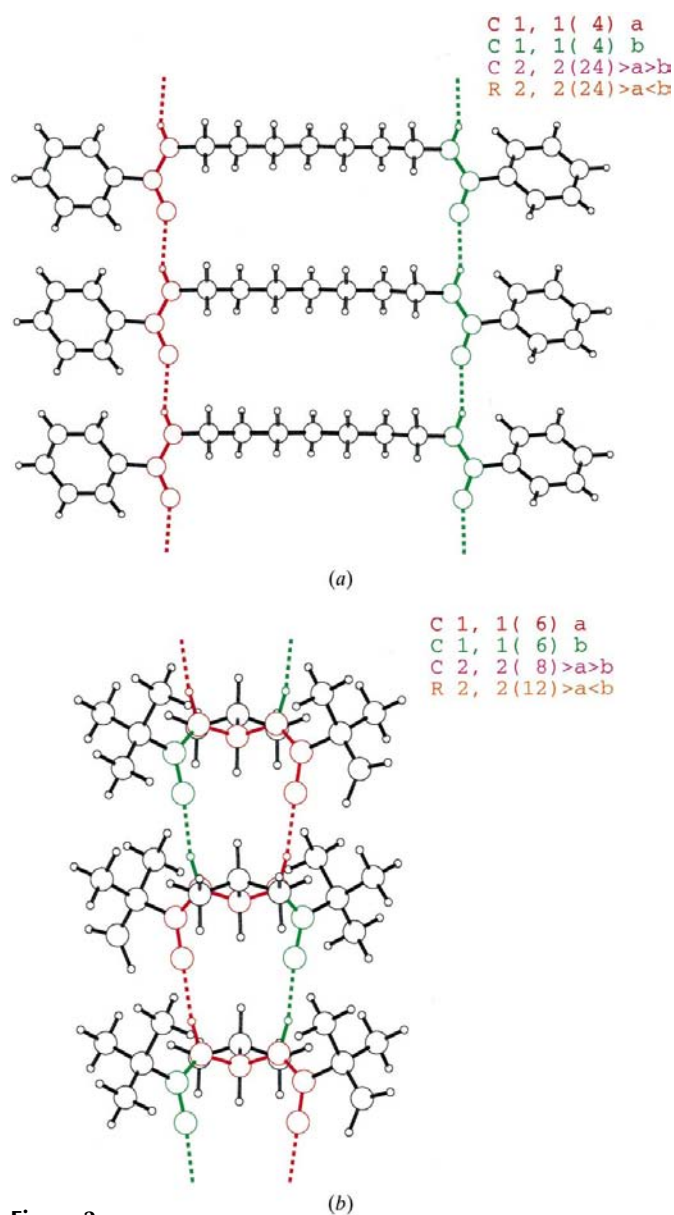


Figure 2 Parallel ladders in (a) *N,N'*-heptamethylenedibenzamide BIWROO, with consecutive hydrogen-bond arrangement; (b) *N*-isobutylidenedipivalamide JOFHOB, with alternating hydrogen-bond arrangement. The first-level chain motifs are highlighted in red and green.

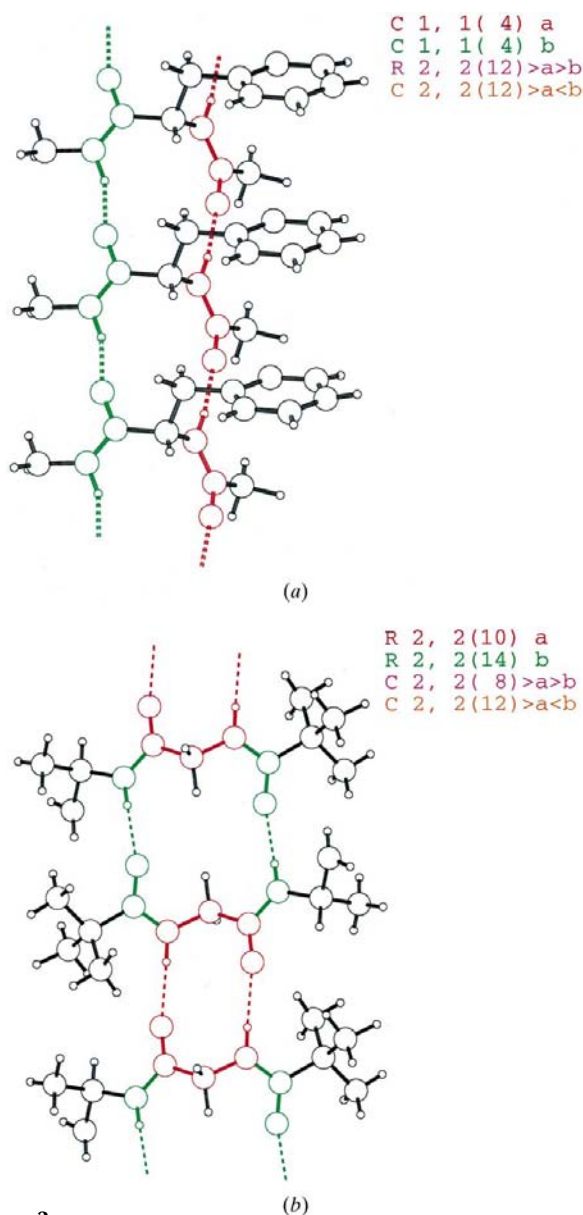


Figure 3 Antiparallel ladders in (a) *N*-acetyl-phenylalanine-*N*-methylamide APALAM, with same-size rings, and (b) *N*-pivalyl-glycyl-isopropylamide PIVGLY, with alternate size rings. The first-level chain motifs are highlighted in red and green.

configuration, with C_6H_4 groups adopting different dihedral angles relative to the amide groups (Table 3). Similarly, the absence of C_i symmetry in ZUKJOE is due to the C_6H_4 groups twisting relative to the central $CH=CH$ group in the same sense. In VISFEI, both ψ and ψ' are $-G$, which also allows approximately antiparallel $C=O$ vectors [$\theta(CO,CO)$ 13.1°, Table 3]. The ladder in PULHUZ is similar, but adjacent molecules are crystallographically independent and related by a pseudo-inversion centre at (0.0015, 0.1244, 0.0018) in Cc .

The type **NO** diamides PIVGLY ($l = 1$, Fig. 3b) and JEPHIV ($l = 5$) differ in that the ladder is comprised of rings of alternating sizes, *i.e.* a graph set **R2,2(2{4 + l}) R2,2(2{6 + l}) C2,2(8) C2,2(2{5 + l})**. In PIVGLY, $C=O$ vectors are at a 152.0° angle, enabling approximately collinear (H)N–C(=O) bonds to be formed, whereas the 115.2° angle in JEPHIV means hydrogen bonds are markedly non-linear. The ladder in LAANMA has similar alternating ring sizes, although adjacent molecules are crystallographically independent and alternate molecules related by a 2_1 screw axis (giving a similar helical twist to ALEUIP), hence a graph set **DDDD; 2[C2,2(8)] 2[C2,2(2{5 + l})] R2,2(2{4 + l}) R2,2(2{6 + l})**. Interestingly, this structure is achieved with a conformation very similar to that of ALEUIP, in which the rings stack in the opposite manner (Harada & Iitaka, 1974). The racemate DLANMA is disordered (each ladder comprises one enantiomer), the major component has the same 4_1 helix structure as ALEUIP, but in the minor component (*ca* 10%) the diamide has the reverse orientation (*i.e.* twofold rotated about an axis perpendicular to the 4_1 axis), such that successive molecules in the stack would be related in the same way as the crystallographically independent molecules in LAANMA. This suggests that helical architectures derived from portions of the PCP and ACP structures are both of comparable energy (Harada & Iitaka, 1974). JEPHOB (**NO**, $l = 4$) also has ladders of alternating ring sizes and two molecules in the asymmetric unit. However, each independent molecule forms a C_i cyclic dimer which then stacks alternately by translation, *i.e.* a 2[**R2,2(2{4 + l})] 2[**D**]; **R2,2(2{6 + l})** arrangement. The chain repeat comprises four independent hydrogen bonds, *i.e.* **C4,4(16)** (Motherwell *et al.*, 1999).**

A large number of diamides of types **OO** and **NN** possess molecular inversion symmetry and form ladders comprised of molecules related by translation, all hydrogen bonds being symmetry-equivalent and the graph set simply being **C1,1(4) [R2,2(2{5 + l})]**. In examples with C_i symmetry, diamide groups are precisely coplanar and $C=O$ vectors necessarily parallel (Tables 2 and 3). However, there are a number of distinct secondary and tertiary structural motifs, *i.e.* the ladders stack in different arrangements, and/or the stacks themselves are arranged differently. The majority of diamides **NN** with straight-chain aliphatic spacers adopt this ladder structure, the chain adopting an all-*anti* conformation having the diamide groups approximately coplanar with the methylene chain [$\varphi(NCO, [CH_2]_n) < 12^\circ$]. These structures possess terminal H, Me, Et or Ph groups: the Ph groups are usually inclined at an angle of *ca* 29° to the diamide group as a result of $C-H \cdots O=C$ repulsion (Harkema *et al.*, 1983). The structures

with $n = 4$ (MEBZAM: $a = 5.118$, $b = 5.324$, $c = 28.41 \text{ \AA}$, $\beta = 97.05^\circ$, Fig. 4b), 6 (BAGJAU10: $a = 5.136$, $b = 5.346$, $c = 31.497 \text{ \AA}$, $\beta = 92.81^\circ$) and 8 (CACHIX: $a = 5.141$, $b = 5.364$, $c = 34.714 \text{ \AA}$, $\beta = 90.57^\circ$) are very closely related, as can be seen from the clear trend in the cell parameters: increasing chain length causes a large increase in the c axis length and a decrease in the β angle, whilst the a and b lengths increase only slightly, and the same packing motif of the tapes is maintained.

Conversely, with terminal H groups, $n = 4$ (TOPPUJ) and $n = 6$ (TOPQAO, Fig. 4c) have structures in $P2_1/c$ which are closely related crystallographically, whilst that of $n = 8$ (TOPQEU) in $P1$ is rather different (Chaney *et al.*, 1996). Interestingly, whilst the ribbons in DAMEDA ($R = Me$, $n = 6$) pack in the same manner as in TOPQEU ($R = H$, $n = 8$) the structure of HEXMPR ($R = Et$, $n = 6$) is closely related to that of TOPQAO ($R = H$, $n = 6$). Of these three packing arrangements, that in DAMEDA and TOPQEU is the simplest: the ladders form stacks approximately in the (120) plane, adjacent stacks being related by translation along both a and b axes perpendicular to the ladder axis c . In HEXMPR, TOPPUJ and TOPQAO, stacks of ladders in (103) are related by a 2_1 axis parallel to the ladder direction, *i.e.* adjacent stacks have the opposite sense and are displaced by $b/2$ relative to each other along the ladder axis (Fig. 4c). Whilst MEBZAM, BAGJAU and CAHCIX have similar stacks of ladders, the 2_1 axes are perpendicular to the ladder direction a , but parallel to the stacking direction b , such that molecules in adjacent stacks form a herringbone arrangement whilst being aligned along the ladder axis a (Fig. 4b). Note that this is not the same orientation of the 2_1 axis as in ZUKJUK (Fig. 4a), in which the screw axis is perpendicular to both the ladder and stack directions.

This ladder structure **C1,1(4) [R2,2(2{5 + l})]** is also exhibited by diamides with aromatic spacer groups, *e.g.* PABZAM, TERSEO and FAPFAD. The terminal Ph rings in PABZAM and TERSEO have a similar conformation to those diamides with aliphatic chains and the aromatic spacer groups make dihedral angles of 30–45° with the amide plane. The secondary packing arrangement in PABZAM differs from those in DAMEDA, HEXMPR and MEBZAM in that successive ladders in the same stack are related by 2_1 axes, *i.e.* of opposite sense and translated by $b/2$, rather than translation. The tertiary structure (the packing of stacks) is the same as in HEXMPR (*i.e.* stacks are related by a 2_1 axis parallel to the ladder axis). Conversely, TERSEO and FAPFAD (which differs from PABZAM only in the replacement of the 4,4'-H atoms by methyl groups) have the same secondary and tertiary structure as DAMEDA. In diacetylhydrazine DIACHZ the ladders are arranged as in PABZAM, but lie on a mirror plane, such that ladders in adjacent stacks lie in an exactly head-to-head manner.

There are fewer examples of diamides **OO** with C_i symmetry, but some do also form the **C1,1(4) [R2,2(2{5 + l})]** ladder structure. Dimethylloxalamide DMOXAM forms the simple stack as in HEXMPR, whilst ETADAM10 [with a $+GA-G$ rather than $AAA (CH_2)_4$ unit] and RAPIQ have

the same packing arrangement as PABZAM. In RAPIYQ, this arrangement presents C—H... π interactions between C₆H₄ groups in adjacent ladders (which are rotated by *ca* 76° with respect to the amide groups). DPTPAM, an isomer of PABZAM with the amide groups reversed, has the same secondary structure as MEBZAM (which also has Ph end groups), although the conformation is similar to that of PABZAM (Table 2).

ZUKKAR (*l* = 10) has a similar arrangement, although crystallographically independent molecules (which differ in the conformation of the amide relative to the C₆H₄C₂C₆H₄

groups) do alternate along the chain, *i.e.* a **DD**; **C2,2(8) R2,2(2{5 + *l*})** ladder. Alternatively, a **C1,1(4) [R2,2(2{5 + *l*})]** ladder may form where the diamide has diad (C₂) symmetry, as does ZALVEN (**OO**, *l* = 3, Table 2). Since adjacent molecules along the chain are related by inversion, the ladder has a zigzag profile, which results in the ladders stacking by translation. The tertiary structure consists of stacks related by a C-centring operation, such that the terminal ⁿBu groups interlock.

3.1.4. Two-dimensional sheet structures and related arrangements. Instead of stacking to form a one-dimensional ladder, some diamides form sheets of the type shown schematically in Fig. 5(b), which is

related to a series of aligned ladders (Fig. 5a) by a displacement of alternate rows of diamide molecules by half the ladder spacing. RAPIYUC (**NN**, *l* = 4) is typical, with hydrogen bonds running parallel and graph set **C1,1(*l* + 5)**, **C1,1(*l* + 5)**, **C2,2(8) C2,2({4 + *l*} + {6 + *l*})**, the network incorporating a complex ring **R($\vec{a} \vec{b} \vec{a} \vec{b}$)** **R4,4 (2{4} + {4 + *l*} + {6 + *l*})**. In the case of RAPIYUC, the diamide probably forms the sheet in preference to the ladder in order for the 1,4-naphthyl group to pack effectively. In the ladder structure, the inter-aromatic spacing would be 4.3 Å, whereas in the sheet structure the closest stacked rings have a more typical separation of 3.46 Å.

These sheets may not necessarily be planar. In RAPIYOW (**OO**, *l* = 6), SAZWEV (**NN**, *l* = 4), BOXFAV (**OO**, *l* = 4), BZOPDA10 (**NN**, *l* = 4), ETBZAM (**NN**, *l* = 2) and diformylhydrazine FOMHAZ (**NN**, *l* = 0; unlike the diacetyl analogue, DIACHZ, which has a ladder structure) the sheets are strongly puckered, forming a 'chevron' arrangement (Palmer & Brisse, 1980). Since the molecules have inversion symmetry, the graph set is **C1,1(4) C1,1(*l* + 5)**, the smallest ring in the network being **R4,4(2{4} + 2{*l* + 5})**, of the form **R($\vec{a} \vec{a}$)₂**. The puckering in RAPIYOW may be in part due to

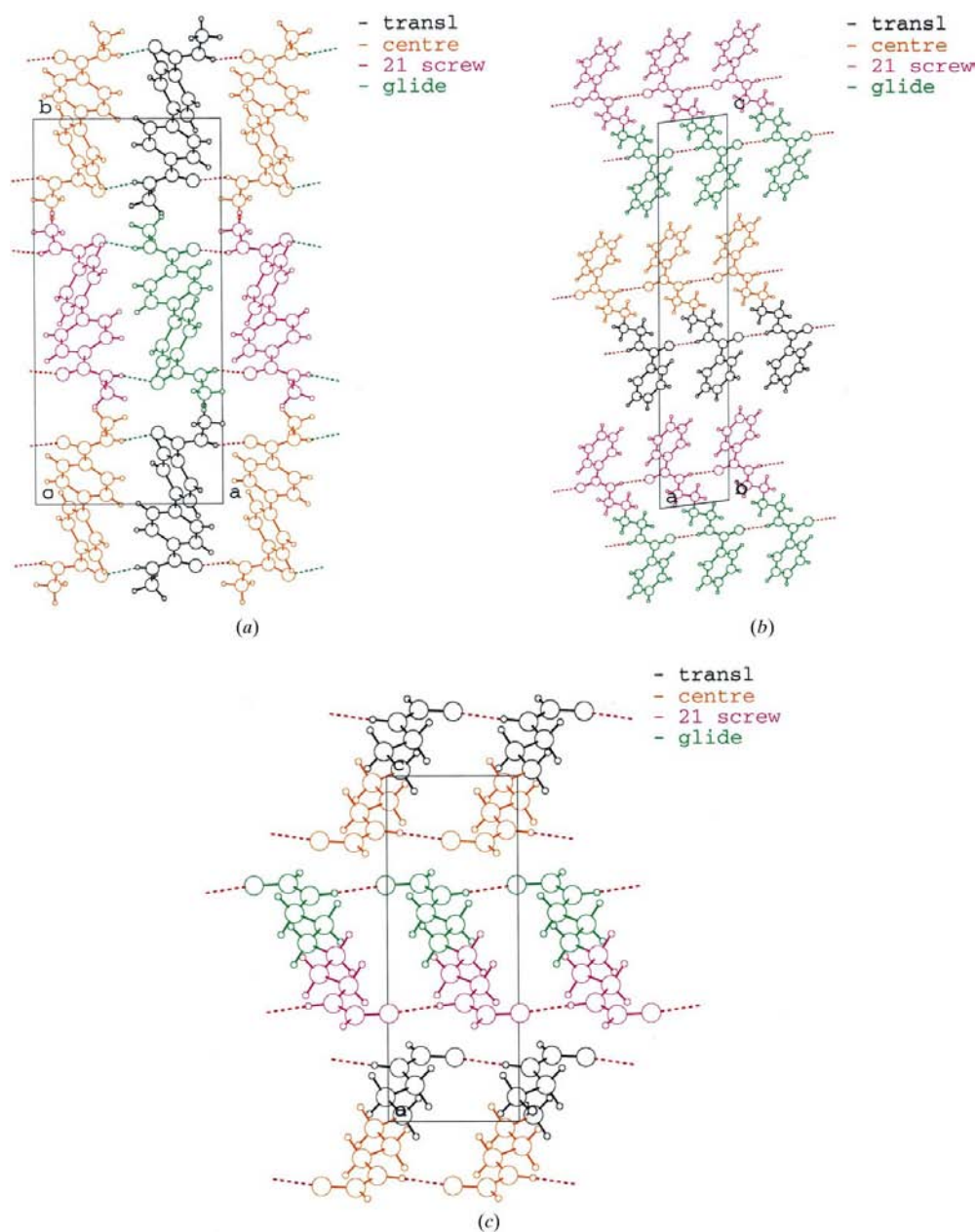


Figure 4

Antiparallel ladder arrangements (a) in *N,N'*-dimethyl-4,4'-biphenyl-dicarboxamide ZURJUK, viewed down the *c* axis, (b) in *N,N'*-tetramethylene-dibenzamide MEBZAM, viewed down the *b* axis and (c) in *N,N'*-hexamethylene-diformamide TOPQAQ, viewed down the *a* axis. Atoms are coloured according to the nature of the symmetry element by which they are generated from the base asymmetric unit (not shown).

an increase in l (there would be a void between the Me groups of molecules in adjacent columns if a planar sheet structure was adopted: Leiserowitz & Tuval, 1978). Conversely, the terminal ${}^t\text{BuC}_6\text{H}_4$ group in SAZWEV is too large for a planar sheet to be formed with only a $(\text{CH}_2)_4$ spacer. Whilst the sheets in RPYOW and SAZWEV stack along \mathbf{a} in $P2_1/c$, BOXFAV, ETBZAM and BZOPDA10 crystallize in $Pbca$, such that adjacent puckered sheets stack by a glide plane rather than by translation.

The reasons for the adoption of a sheet rather than a ladder structure for type **OO** and **NN** diamides with l even are not entirely clear. Whilst the sheet is only observed in structures with $l = 0-6$, the ladder is also found for longer spacer groups with $l = 0-10$. The relative length of the spacer X to the size of the terminal groups R is important, since if the length of X is not well matched to the size of R , the degree of puckering increases in the sheet structure. Interestingly, PABZAM and BZOPDA10 could be considered as polymorphs with the ladder and sheet structures, respectively, although the conformations differ somewhat (the C_6H_4 spacer is twisted by a further 20° in sheet structure relative to the amide groups). Harkema *et al.* (1983) suggested that the more twisted C_6H_4 group allows shorter hydrogen bonds to form in the sheet structure, whereas the ladders packed more efficiently, giving a lower-density structure. The crystallization conditions may be significant: whereas the sheet structure was crystallized by vacuum sublimation at 600 K (Adams *et al.*, 1978), the ladder polymorph was recrystallized from dimethylacetamide (Harkema & Gaymans, 1977).

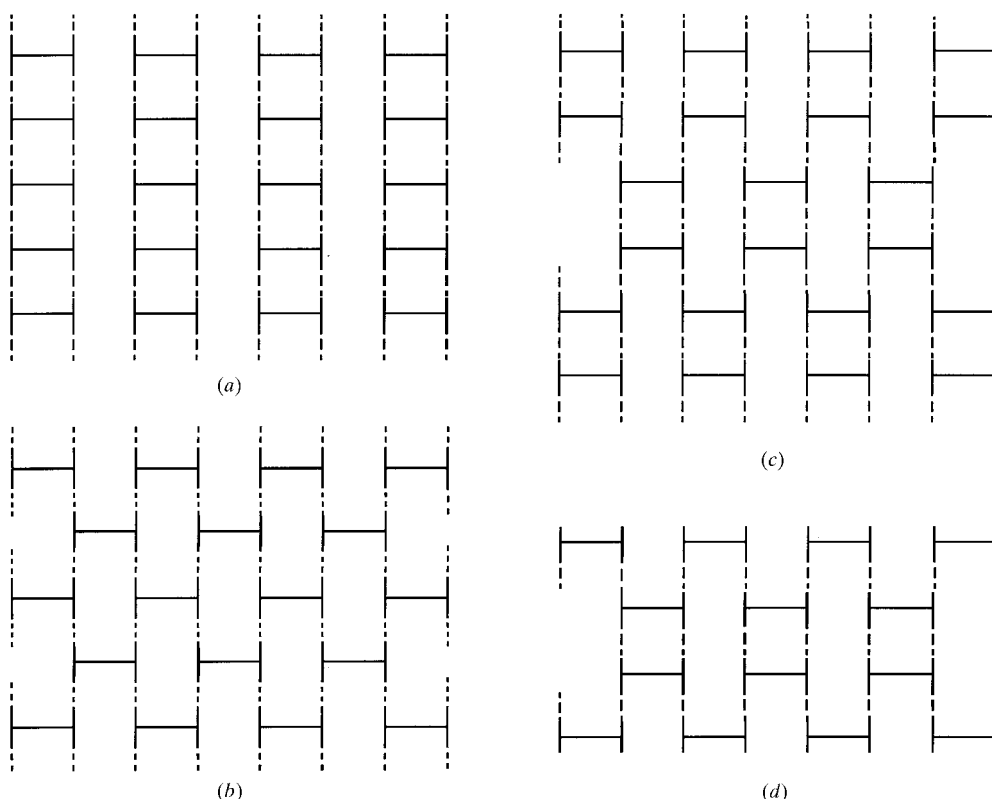


Figure 5
Schematic representation of (a) ladder, (b) 1:1 sheet, (c) 2:2 sheet and (d) 2:2 tape structures.

In JUDZEN (**NO**, $l = 1$) the amide groups are aligned parallel, but the $\text{C}(=\text{CH}_2)$ spacer does not allow a ring to be formed on both sides of the diamide: instead, a 2:2 sheet structure is formed which could be considered as being derived from parallel ladders (Fig. 5a) by moving pairs of rows by half of the ladder spacing (Fig. 5c). ALNMAM and NALEUE have a similar sheet structure, but only one molecule in the asymmetric unit. The graph set is then **R**2,2(2{4 + l }) **C**1,1(6 + l), **C**2,2(8) **C**2,2(2{5 + l }), the ring typically exhibiting C_i symmetry. The conformation of these molecules is similar to those of LAANMA, DLANMA and ALEUIP, which form twisted ladders, although ψ is smaller and $\theta(\text{CO},\text{CO})$ significantly larger (Table 1). Since JUDZEN comprises two crystallographically independent molecules, the graph set becomes **DD** **C**1,1(6 + l) **C**1,1(6 + l); **R**2,2(2{4 + l }) (ignoring the second level discrete patterns), the **C**4,4(16) being a fourth level $\text{C}(\vec{a} \vec{b} \vec{c} \vec{d})$ pattern. The planarity of the intramolecular conformation in JUDZEN by comparison with ALNMAM and NALEUE results in much flatter sheets.

The structure of POLNIN (Fig. 6) is based on that of JUDZEN, but the more bulky $X = \text{C}(\text{Ph})_2$ spacer prevents the formation of a planar sheet. The puckered tape structure (Fig. 5d) is derived from the sheet (Fig. 5c) in JUDZEN by breaking the hydrogen-bonded rings between every alternate row and dividing the sheet into tapes. In this case, the **R**2,2(10) rings have diad symmetry, such that the graph set for the tape is **DD** **R**2,2(2{5 + l }); **C**2,2(2{6 + l }).

EDACTM10 (**NN**, $l = 1$) is $-GA$, rather than $-G-G$ or $-G+G$ conformation, which gives $\theta(\text{CO},\text{CO}) \simeq 60^\circ$ and an amide interplanar angle of 85° . As a consequence, mutually perpendicular **C**1,1(4) chains are formed along \mathbf{b} and \mathbf{c} , leading to second-level patterns 2[**R**4,4(4{5 + l })]. This generates a sheet in the bc plane (Fig. 7), the sheets stacking by translation along \mathbf{a} , which is quite different from the sheet structure in RPYUC.

3.1.5. Three-dimensional network structures. Three-dimensional networks are typically formed when the angles between the $\text{C}=\text{O}$ vectors approach 90° . AGLYPR and NAAIBA (**NO**, $l = 1$) are typical examples, with graph sets **C**1,1(4 + l) **C**1,1(6 + l); **C**2,2(8) **C**2,2(4 + l){6 + l }. Note that since the graph-set description is purely topological, it is not possible to deduce from the first- and second-level graph sets whether the network is three-dimensional or not, as it is also necessary to consider the directions along which the chains are

propagated in the crystal. The conformation of AGLPYR is similar to those of LAANMA, DLANMA and ALEUIP, which form twisted ladders, although the inter-carbonyl angle is somewhat smaller. NAAIBA has a conformation most similar to POLPIP, although the $\text{NH}\cdots\text{N}$ contact is longer (2.47 Å) and the *R* groups smaller, allowing two chains to be formed. The related molecule TIRJIN, however, forms a ladder structure (see above), despite having a similar (+*G*–*G*) conformation to NAAIBA. Whilst NAKLOA (**NO**, *l* = 3) might be expected to form a similar ladder motif to JEPHIV, since the $\text{C}=\text{O}$ vectors are approximately antiparallel, it also has a $\text{C}1,1(4+l) \text{C}1,1(6+l); \text{C}2,2(8) \text{C}2,2(\{4+l\}\{6+l\})$ structure. Conversely, DEBHEX (**NO**, *l* = 1, –*GA*) forms

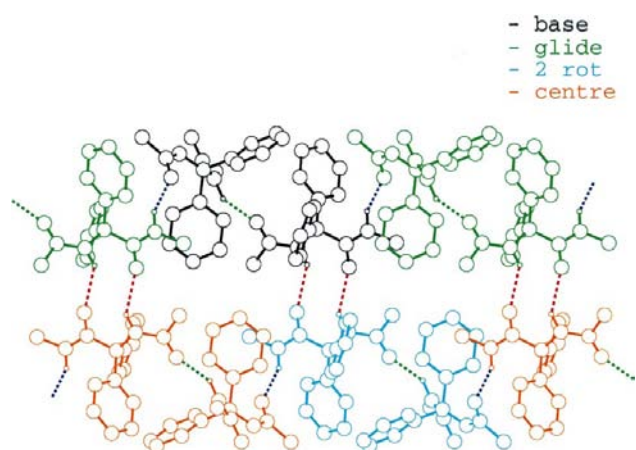


Figure 6
Hydrogen-bonded tape structure of *N*-acetyl-2,2-diphenylglycyl-*N*-methylamide POLNIN, showing alternating dimers and monomers; atoms are coloured according to the symmetry operator relating them to the two molecules in the base asymmetric unit. H atoms not involved in hydrogen bonds are omitted for clarity.

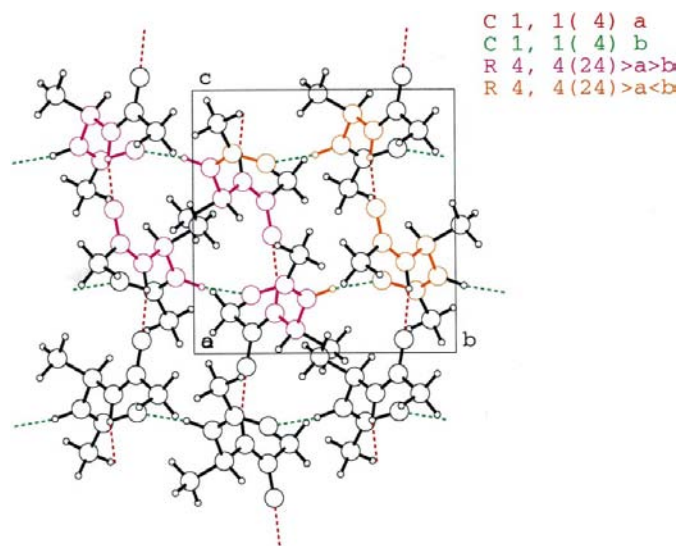


Figure 7
Hydrogen-bonded sheet structure of ethylidene-*N,N'*-diacetamide EDACTM10, with perpendicular chains of hydrogen bonds, highlighting the second-level $\text{R}4,4(24)$ rings in magenta and orange.

hydrogen bonds between the same amide groups, thus giving a graph set of $\text{C}1,1(4) \text{C}1,1(4); \text{C}2,2(2\{5+l\}) \text{C}2,2(\{4+l\}\{6+l\})$.

The structure of JOFHIV (**NN**, *l* = 1) is related to that of JUDZEN in that it is derived from the 2:2 sheet structure (Fig. 5c, which it resembles in projection), with a given ring linked to two other rings in different sheets rather than the same ring in the same sheet. Since there are two independent molecules in the asymmetric unit, the graph set for this arrangement is **DDDD**; $2[\text{C}2,2(8)] 2[\text{C}2,2(2\{5+l\})] 2[\text{R}2,2(2\{5+l\})]$. The conformation is very different from that of the diamides **NN** JOFHOB and HEYREI, both angles being *G* of the same sign, such that the $\text{C}=\text{O}$ groups are approximately antiparallel rather than parallel. Unlike JUDZEN, it is unclear why a ladder is not formed as there is no significant steric hindrance. In YEKCIA (**OO**, *l* = 3), pairs of molecules are joined by an $\text{R}2,2(16)$ ring about a diad axis, and pairs of molecules related by a 4_1 axis are joined to form $\text{C}1,1(8)$ chains along *a* and *b*, giving an overall $\text{R}2,2(2\{5+l\}), \text{C}1,1(5+l); \text{C}2,2(8) \text{C}2,2(2\{5+l\})$ arrangement.

3.2. Triamide structures

3.2.1. Chain structures. Conformational and structural data for tri- and polyamides are summarized in Table 4. ZADJET forms a simple $\text{C}(2l+6)$ chain structure, one $\text{S}(2l+8)$ ring being formed, whilst the other donor and acceptor form no $\text{N}-\text{H}\cdots\text{O}=\text{C}$ hydrogen bonds. The closely related structures with fewer bulky substituents, ZADJAP and ZADHUH, form ladder and sheet structures, respectively.

3.2.2. Ladder structures. NUSDOU forms a bi-ladder structure in which all the hydrogen bonds are utilized (Fig. 8). The structure is closely analogous to that of PIVGLY and represents a larger portion of the PCP motif. Adjacent molecules in the ladder are related by a 2_1 screw axis, such that

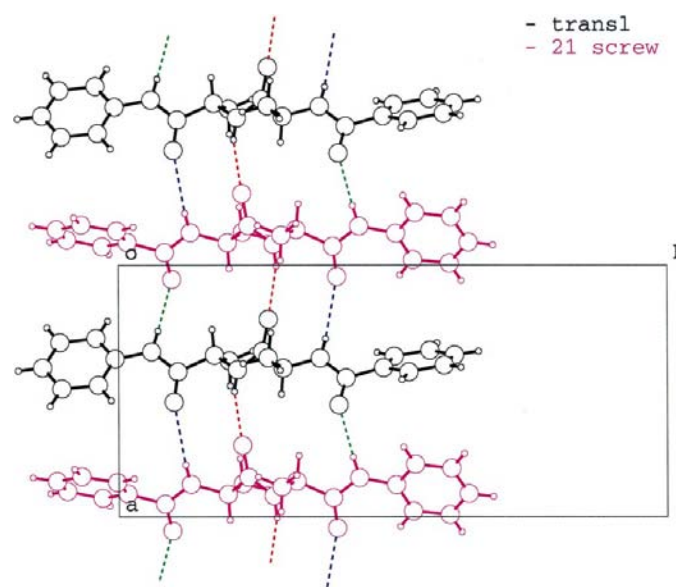


Figure 8
Bi-ladder structure parallel to the *a* axis in *N*-benzoyl-alanyl-*N*-phenylalaninamide NUSDOU, representing a slice of the PCP polypeptide sheet.

Table 4
Tri-, tetra- and penta-amides.

<i>n</i>	Refcode	X^2, X^2	R^1, R^2	Graph set	ω_1 ($^\circ$)	τ_1 ($^\circ$)	τ_2 ($^\circ$)	ω_2 ($^\circ$)	$\tau(\text{NCO}, \text{NCO})$ ($^\circ$)	$\theta(\text{CO}, \text{CO})$ ($^\circ$)
(i) $R^1[\text{C}(=\text{O})\text{NH}-X-]_n\text{C}(=\text{O})\text{NH}R^2$										
2	CEYLIB	CH ₂ CH ₂	^t Bu ⁱ Pr	C1,1(4)<i>a</i>, C1,1(8)<i>b</i>, S1,1(10)<i>c</i> C2,2(10)$\vec{a} \vec{b}$, C2,2(12)$\vec{a} \vec{b}$	-169 176	φ -68 -89	ψ -25 3	176 -176	75.0 (1-2) 86.8 (2-3) 56.6 (1-3)	51.6 (1-2) 66.9 (2-3) 41.9 (1-3)
2	CEYLOH	CHMe CH ₂	^t Bu ⁱ Pr	R2,2(10)<i>a</i>, C1,1(5)<i>b</i>, S1,1(10)<i>c</i> C2,2(12)$\vec{a} \vec{b}$, $\vec{a} \vec{b}$	-174 -177	-68 83	132 2	-177 179	89.6 86.4 50.8	113.3 62.9 51.4
2	KUJZOE	CH ₂ CH ₂	^t Bu cy-C ₆ H ₁₁	Da - l R2,2(12)$\vec{a} \vec{b}$, $\vec{f} \vec{k}$ R2,2(15)$\vec{c} \vec{d}$, $\vec{e} \vec{f}$, $\vec{h} \vec{i}$, $\vec{g} \vec{l}$ C2,2(8)$\vec{c} \vec{f}$, $\vec{i} \vec{l}$ C2,2(12)$\vec{d} \vec{e}$, $\vec{g} \vec{h}$ C2,2(15)$\vec{c} \vec{e}$, $\vec{d} \vec{f}$, $\vec{g} \vec{i}$, $\vec{h} \vec{l}$	-169 -175 -173 -172 -173 -174 -175 -178	-117 -83 -81 96 -79 106 -118	-4 158 -17 171 -20 165 -2	-175 175 -172 -179 -174 173 -178	64.9, 87.2 48.4 87.9, 82.6, 71.4 87.8, 77.0 75.2 64.9, 87.1 43.9	61.5, 114.3 53.0 47.0, 104.6 140.6 43.3, 106.3 141.7 64.8, 112.3 47.5
2	NUSDOU	CHMe CHMe	Ph Ph	C1,1(4)<i>a</i>, C1,1(8)<i>b</i>, C1,1(10)<i>c</i> R2,2(10)$\vec{a} \vec{b}$ C2,2(12)$\vec{a} \vec{b}$, $\vec{a} \vec{c}$ R2,2(14)$\vec{a} \vec{c}$ C2,2(8)$\vec{b} \vec{c}$, R2,2(18)$\vec{b} \vec{c}$	174 176	-156 -146	141 154	176 177	40.1 33.8 12.6	160.9 172.4 13.6
2	VOKCON	CHMe C=CHPh Molecule B	^t Bu ⁱ Pr	D1,1(2)<i>a,b,d,g,h</i> S1,1(10)<i>c,f,i</i> R2,2(14)<i>e</i> R4,4(24)$\vec{a} \vec{b}$ C2,2(12)$\vec{g} \vec{h}$	176 -172 -178 174 165 -177	-68 106 -64 76 67 -90	118 -5 135 8 -132 5	-172 -179 174 -176 -177 175	86.2, 67.5 54.2 86.8, 59.3 75.8 88.3, 85.5 33.6	125.1, 76.0 49.4 113.6, 56.1 60.5 106.4, 70.9 37.9
2	ZADHUH	CMePh CHCH ₂ Ph	Ph cy-C ₆ H ₁₁	C1,1(4)<i>a</i>, C1,1(8)<i>b</i>, S1,1(10)<i>c</i> C2,2(10)$\vec{a} \vec{b}$, C2,2(12)$\vec{a} \vec{b}$	-174 -176	50 -90	-130 4	-176 177	76.2, 86.4 43.4	107.1, 67.8 40.5
2	ZADJAP	CMe ^t Pr CHCH ₂ Ph	Ph cy-C ₆ H ₁₁	C1,1(4)<i>a,b</i>, C1,1(5)<i>c</i> R2,2(12)$\vec{a} \vec{b}$, C2,2(12)$\vec{a} \vec{b}$ C2,2(9)$\vec{a} \vec{c}$, R1,2(7)$\vec{a} \vec{c}$ R2,2(15)$\vec{b} \vec{c}$, C2,2(15)$\vec{b} \vec{c}$	173 174	70 -157	40 117	174 172	87.6, 58.4 51.9	33.9, 145.8 114.7
2	ZADJET	CMeCH ₂ Ph CHCH ₂ Ph	Ph cy-C ₆ H ₁₁	C1,1(8)\vec{a} S1,1(10)\vec{b}	-171 -176	-60 -90	-24 -2	-176 179	67.0, 89.3 58.5	46.3, 71.7 46.5
2	NUSDOU	CHMe CHMe	Ph Ph	C1,1(4)<i>a</i>, C1,1(8)<i>b</i>, C1,1(10)<i>c</i> R2,2(10)$\vec{a} \vec{b}$ C2,2(12)$\vec{a} \vec{b}$, $\vec{a} \vec{c}$ R2,2(14)$\vec{a} \vec{c}$ C2,2(8)$\vec{b} \vec{c}$, R2,2(18)$\vec{b} \vec{c}$	174 176	-156 -146	141 154	176 177	40.1, 33.8 12.6	160.9, 172.3 13.6
3	JORKIK	C=CHPh CH ^t Pr C=CHPh	Me Me	C1,1(8)<i>a,b</i>, S1,1(10)<i>c,d</i> C2,2(16)$\vec{a} \vec{b}$ R2,2(12)$\vec{a} \vec{b}$	-175 177 170	-54 -62 -59	-24 -20 -24	177 170 -176	-	-
(ii) $R^1\text{NHC}(=\text{O})-X-\text{C}(=\text{O})\text{NH}-X-\text{C}(=\text{O})\text{NHR}^2$										
2	VEGXUA	CH ₂ CH ₂	Me Me	C1,1(4)<i>a</i>, C1,1(5)<i>b</i>, C1,1(7)<i>c</i> C2,2(15)$\vec{a} \vec{b}$, $\vec{a} \vec{b}$, $\vec{a} \vec{c}$, $\vec{a} \vec{c}$ C2,2(8)$\vec{b} \vec{c}$, C2,2(12)$\vec{b} \vec{c}$	180 179	105 -73	112 153	179 180	79.8, 86.5 88.3	115.9, 114.3 129.8
(iii) $R^1\text{C}(=\text{O})\text{NH}-X-\text{NHC}(=\text{O})-X-\text{C}(=\text{O})\text{NHR}^2$										
	JEYFOI	CHMe CH ₂	^t Bu ⁱ Pr	C1,1(4)<i>a</i>, C1,1(6)<i>b,c</i> C2,2(16)$\vec{a} \vec{b}$, $\vec{a} \vec{b}$ C2,2(8)$\vec{b} \vec{c}$, R2,2(12)$\vec{b} \vec{c}$ C2,2(14)$\vec{a} \vec{c}$, $\vec{a} \vec{c}$	-179 170	-111 150	107 125	170 174	61.5, 73.8 62.0	25.4, 75.6 85.6

the first level motifs are **C1,1(4)** **C1,1(6 + 2*l*)** **C1,1(8 + 2*l*)**. Pairs of molecules are linked by both smaller and larger rings which alternate along the chain: the full second-level graph set being **R2,2(2{4 + *l*})** **C2,2(2{5 + *l*})** **R2,2(2{6 + *l*})** **C2,2(2{5 + *l*})** **C2,2(8)** **R2,2(2{7 + 2*l*})** (the envelope of the two smaller rings). This arrangement is possible because the conformation of the molecule is such that adjacent C=O groups are approximately parallel. Conversely, ZADJAP has a **C1,1(4)** **C1,1(4)** **C2,2(2{5 + *l*})** **R2,2({4 + *l*}{6 + *l*})** ladder structure closely related to that of ALEUIP, although the helical twist occurs about a 6₁ rather than 4₁ axis. In addition, one C=O group is

bifurcated and forms a hydrogen bond to the third NH group, giving a **C1,1(4 + *l*)** chain at first level (Table 4), the third acceptor forming no hydrogen bonds.

3.2.3. Sheet structures. Sheet structures, rather than three-dimensional architectures, are formed when all intermolecular hydrogen bonds propagate in the same plane. VEGXUA (Fig. 9) is a good example: molecules are related by translation along **c** by **C1,1(4)** and by **C1,1(4 + *l*)** and **C1,1(6 + *l*)** in the **ac** plane *via* 2₁ axes, such that the latter chains run along the (10 $\bar{1}$) and (101) directions, respectively. In fact, the **C1,1(4)** chains along (001) are not necessary to the integrity of the sheet

structure, and if these are ignored the network is reminiscent of that in the diamide ETACTM10 (Fig. 7), although the symmetry relationships are quite different. NICJUE has a similar extended structure, but with a simpler graph set description $3[\mathbf{C}1,1(5+l)]; 3[\mathbf{C}2,2(\{4\}\{5+l\}) \mathbf{C}2,2(\{4+l\}\{6+l\})]$, the simpler $\mathbf{C}3,3(12)$ chain appearing at the third level.

The sheet structure in KUJZOE is rather more complicated, largely because of the presence of four molecules in the asymmetric unit, pairs of which have essentially the same conformations. As a result, the first-level graph sets for the 12 crystallographically independent hydrogen bonds are all \mathbf{D} (Table 4). Pairs of molecules with different conformations alternate in ladders, joined by $\mathbf{R}2,2(15)$ rings. The sheet is composed of two crystallographically independent ladders of this type, which are cross-linked by the remaining hydrogen bonds forming two crystallographically independent $\mathbf{R}2,2(12)$ rings.

VOKCON, with three molecules *A*, *B* and *C* in the asymmetric unit, also forms complex sheets. The independent molecules have essentially equivalent conformations and form the same intramolecular $\mathbf{S}(2l+8)$ rings. Pairs of molecule *B* form an $\mathbf{R}2,2(14)$ ring about an inversion centre, this $\mathbf{C}=\text{O}$ acceptor also forming one of the intramolecular bonds. These dimers stack along *c* and are joined by two *C_r*-related molecules *A* to form $\mathbf{R}4,4(24)$ second-level rings and hence ladders composed of molecules *A* and *B*. The third independent molecule *C* links these ladders by forming two hydrogen bonds to *A* [hence a $\mathbf{C}2,2(2\{5+l\})$ graph set] and one hydrogen bond to *B* (one acceptor on *C* not being used in hydrogen-bond formation). A ring of the type $\mathbf{R}(\vec{a} \vec{b} \vec{c})$ is thus formed between one of *A*, *B* and *C*, two of one enantiomer and one of the other.

Sheet structures may also be formed by triamides when one donor and acceptor are used to form an intramolecular hydrogen bond. CEYLIB and ZADHUH are good examples: the central amide group forms a chain along *b* (CEYLIB) or *a* (ZADHUH) and the terminal amide groups form an intra-

molecular bond and chain along *c* (CEYLIB) or *b* (ZADHUH) to form a sheet similar to that in VEGXUA (Fig. 9), with the graph set $\mathbf{C}1,1(4) \mathbf{C}1,1(6+2l) \mathbf{S}(8+2l); \mathbf{C}2,2(2\{4+l\}) \mathbf{C}2,2(2\{5+l\})$. CEYLIB and ZADHUH differ in that adjacent molecules in the $\mathbf{C}1,1(6+2l)$ chain are related by translation in ZADHUH, but by a glide plane in CEYLIB; similarly sheets stack by translation in ZADHUH and by a glide plane in CEYLIB. The analogue CEYLOH forms a similar intramolecular ring, but the chain conformation differs and this permits centrosymmetric ring dimers to form, which are linked by the other hydrogen bond that forms a chain along *b* via a 2_1 axis (Fig. 10), to give an overall $\mathbf{C}1,1(4+l) \mathbf{R}2,2(2\{4+l\}) \mathbf{S}1,1(8+2l); \mathbf{C}2,2(2\{5+l\}) \mathbf{C}2,2(\{4\}\{6+2l\})$ pattern. PVMGLA ($l=1, l'=2$) also has one *S*, *C* and *R* motif at the first level: the full graph set is $\mathbf{C}1,1(6+l) \mathbf{R}2,2(2\{5+l+l'\}) \mathbf{S}1,1(5+l'); \mathbf{C}2,2(\{4\}\{6+l+l'\}), \mathbf{C}2,2(\{4+l'\}\{6+l+l'\})$. The ring dimers are generated by a diad along *c* and the chain propagated by a 2_1 axis along *b*.

3.2.4. Three-dimensional networks. Some three-dimensional networks are based on a ladder structure formed from two hydrogen bonds, the other hydrogen bond linking the ladders. JEYFOI is a good example: two hydrogen bonds form a ladder of the same $2[\mathbf{C}1,1(\{5+l\}); \mathbf{C}2,2(8) \mathbf{R}2,2(\{4+l\}\{6+l\})$ type as in JOFHOB, successive molecules being related by a 2_1 axis. These ladders are then cross-linked by a $\mathbf{C}1,1(4)$ chain running perpendicular to the ladder axis. BAFLOJ also has a three-dimensional network (Table 4) with a second-level $\mathbf{R}4,4(2\{4+l\} + 2\{6+l\})$ pattern.

3.3. Polyamide structures

JORJIK (Table 4) forms two intramolecular hydrogen bonds and thus has only two donors and acceptors available for hydrogen bonding, with the result that a $2[\mathbf{C}1,1(6+2l)] 2[\mathbf{S}1,1(8+2l)]; \mathbf{C}2,2(\{4+l\}\{8+2l\}) \mathbf{R}2,2(2\{5+l\})$ ladder is formed, which is similar to that in the diamide ALEUIP,

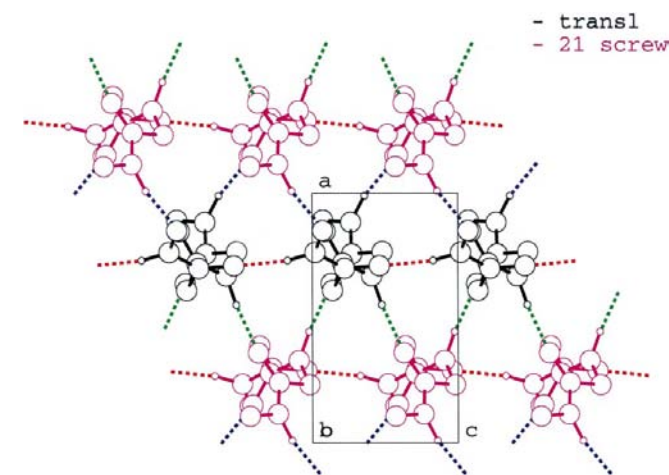


Figure 9
Sheet structure of *N*-methyl-glycyl-glycylmethylamide VEGXUA, composed of three independent non-parallel chains of hydrogen bonds (red, blue and green), viewed down the *b* axis.

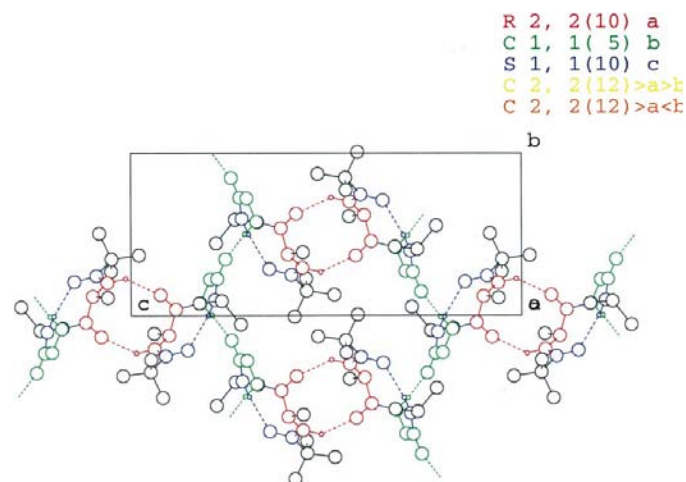


Figure 10
Sheet structure of pivaloyl-alanyl-*N*-isopropylglycinamide CEYLOH, viewed down the *a* axis, composed of linked centrosymmetric $\mathbf{R}2,2(10)$ rings (red) cross-linked by the $\mathbf{C}1,1(5)$ chain (green); the intramolecular $\mathbf{S}1,1(10)$ ring also shown (blue). H atoms not involved in hydrogen bonds are omitted for clarity.

Table 5

Graph-set matrix for JUHJEB.

 \vec{a} motifs on leading diagonal, $\vec{a} \vec{b}$ patterns in top right, $\vec{a} \overleftarrow{b}$ in bottom left.

	a	b	c	d	e
a	C1,1(4)	C2,2(12)	C2,2(20)	C2,2(26)	C2,2(34)
b	C2,2(12)	C1,1(4)	C2,2(14)	C2,2(20)	C2,2(28)
c	C2,2(20)	R2,2(14)	C1,1(4)	C2,2(12)	C2,2(20)
d	C2,2(26)	C2,2(20)	C2,2(12)	C1,1(4)	C2,2(14)
e	C2,2(34)	C2,2(28)	C2,2(20)	R2,2(14)	C1,1(4)

although the helical twist is about a 2_1 rather than a 4_1 axis, so that the rings are more strongly twisted. ZADHER only uses two acceptors and three donors in N–H...O=C bonding, forming two intramolecular bonds and one C1,1(11) chain (one of the acceptors is bifurcated). Similarly, ZADHOB forms only one intermolecular pattern, a C1,1(10) chain, and two intramolecular rings, but without bifurcation.

The structure of the penta-amide JUHJEB is rather more interesting. The full graph-set matrix is given in Table 5. The two-dimensional network in space group Cc consists of sheets, in which the molecular axis is perpendicular to the sheet. This is composed of two parallel ladders, which relate molecules along the (110) and ($\bar{1}\bar{1}0$) directions *via* the C -centring operation, and a C1,1(4) chain, which relates molecules by translation along **b**. These sheets are then stacked *via* the c -glide operator.

3.4. Polymeric amide structures

Many of the diamide compounds were originally studied as model systems for the structures of synthetic polyamide fibres or polypeptides in biological systems. The polymers nylon 6,6 (HICWOF) and nylon 6,10 (HICWUL) contain the same motifs as observed in the straight-chain aliphatic diamides **OO** and **NN** discussed above. Since the chains have the same C_i symmetry, the graph sets are similar, *viz.* C1,1(4) [R2,2(18), R2,2(22)] for 6,6 and C1,1(4) [R2,2(22), R2,2(26)] for 6, 10, respectively, the sheets being stacked by translation. Similarly, nylon 7,7 (WIMTER) has a PCP structure and is clearly closely related to BIWROO, although the methylene chains deviate much less from the plane of the amide groups. Since there is mirror symmetry perpendicular to the polymer length, the graph set is C1,1(4) [R2,2(20), R2,2(24)].

Poly(*p*-phenylene terephthalamide) HIDDUT could be considered as a sheet formed by fusing alternating ladders as found in DPTPAM and PABZAM (Table 2). If the space group is taken as being $P2_1/n$ (rather than Pn) the first-level basic graph set is C1,1(4) 2[R2,2(18)]. The phenylene rings are twisted in opposite senses with respect to the amide plane, that between the NH groups by 38° , more than between the C=O groups (30°). SUSHUJ is a mixed aromatic/aliphatic polymer also having a flat sheet structure, with alternating 1,3-(CH₂)₂C₆H₄ (between NH) and (CH₂)₄ (between C=O) spacer groups, the asymmetric unit comprising the 1,3-xylylene and two halves of two butylene groups.

4. Conclusions

4.1. Peptides and retropeptides ($n = 1$)

The diamide structures discussed in this paper exhibit a significant degree of conformational flexibility, which allows a large number of alternative hydrogen-bond motifs to be adopted, which are not easy to rationalize simply from a knowledge of the identity of the X and R groups. For true peptides **NO**, a parallel arrangement of the C=O groups, which allows the formation of parallel ladders, is rare (occurring only in TIRJIN) and this requires a + G + G (or – G – G) peptide conformation, similar to that in NAABIA which instead forms a three-dimensional network. Dihedral angles of $-\psi \simeq \varphi \simeq 105^\circ$ orient the diamide groups to allow an antiparallel ladder arrangement to be formed. The ladders may comprise the same size or alternating size rings, mimicking portions of the PCP and ACP peptide structures, respectively, whilst for retropeptides this conformation provides a parallel ladder and the rings are necessarily the same size (*e.g.* JOFHER, HEYREI). If the peptide is twisted such that φ approaches $-G$ and ψ tends to A , the ladders of either type adopt a corresponding helical twist. If the twist is slightly greater, a three-dimensional network typically results (DEBHEX, NAABIA). Sheet structures tend to occur if the formation of two rings is sterically blocked, *e.g.* if X is a planar carbon or has bulky substituents: in extreme cases, one donor and acceptor may form no intermolecular hydrogen bonds at all, and the other donor and acceptor form a ring or chain motif (*e.g.* POLPEL, POLPIP). Polyamides are considerably more complicated because of the greater number of hydrogen-bonding possibilities and there are so few examples that they need to be considered individually. However, some of the structural motifs present in the diamide structures are carried over to the polyamides, and the ladders in NUSDOU and JUHJEB are particularly notable in this respect.

4.2. Diamides with straight-chain aliphatic and aromatic spacers ($n \geq 2$)

The majority of structures of type **OO** and **NN** diamides with aromatic or (CH₂) _{n} spacers (where n is even) fall into two clear classes: antiparallel ladder and sheet arrangements. The ladder arrangement is more tolerant of the nature of the X and R groups, the degree of pucker and the sizes of the two groups. In both arrangements, molecules with C_i symmetry generally lie on a crystallographic inversion centre. For diamides with certain X and R groups, polymorphs with both architectures are observed experimentally. For the ladder network, five different packing arrangements are observed for the ladders, whereas only two are represented for the less-common sheet structures.

The structures with l odd are closely related to the corresponding retropeptides, *e.g.* BIWROO is similar to JOFHER with a PCP-type motif. Similarly, diamide **NO** (JEPHIV) has the same ladder ACP (alternate) ring ladder arrangement as the peptide PIVGLY. For both $l = \text{odd}$ and $l = \text{even}$, the corresponding polymers are closely based on the ladder

structures and the polymer sheets are stacked in similar arrangements to the ladders.

References

- Aakeroy, C. B. (1997). *Acta Cryst.* **B53**, 569–586.
- Aakeroy, C. B., Nieuwenhuyzen, M. & Price, S. L. (1998). *J. Am. Chem. Soc.* **120**, 8986–8993.
- Aakeroy, C. B. & Seddon, K. R. (1993). *Chem. Soc. Rev.* **22**, 397–407.
- Adams, W. W., Fratini, A. V. & Wiff, D. R. (1978). *Acta Cryst.* **B34**, 954–956.
- Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37.
- Bernstein, J. (1991). *Acta Cryst.* **B47**, 1004–1010.
- Bernstein, J., Davis, R. E., Shimoni, L. & N.-L. Chang (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Bernstein, J., Etter, M. C. & MacDonald, J. M. (1990). *J. Chem. Soc. Perkin Trans. II*, pp. 695–704.
- Brisson, J. & Brisse, F. (1982). *Acta Cryst.* **B38**, 2663–2667.
- Bruno, I. J., Cole, J. C., Lommerse, J. P. M., Rowland, R. S., Taylor, R. & Verdonk, M. L. (1997). *J. Comput. Aided Mol. Des.* **11**, 525–537.
- Bunn, C. W. & Garner, E. V. (1947). *Proc. R. Soc. London Ser. A*, **189**, 39–68.
- Chaney, J. D., Goss, C. R., Folting, K., Santarsiero, B. D. & Hollingsworth, M. D. (1996). *J. Am. Chem. Soc.* **118**, 9432–9433.
- Coupar, P. I., Glidewell, C. & Ferguson, G. (1997). *Acta Cryst.* **B53**, 521–533.
- Desiraju, G. R. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 2311–2327.
- Desiraju, G. R. (1997). *Chem. Commun.* pp. 1475–1482.
- Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
- Etter, M. C. (1991). *J. Phys. Chem.* **95**, 4601–4610.
- Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* **B46**, 256–262.
- Ferguson, G., Bell, W., Coupar, P. I. & Glidewell, C. (1997). *Acta Cryst.* **B53**, 534–543.
- Ferguson, G., Coupar, P. I. & Glidewell, C. (1997). *Acta Cryst.* **B53**, 513–520.
- Ferguson, G., Glidewell, C., Gregson, R. M. & Meehan, P. R. (1998a). *Acta Cryst.* **B54**, 129–138.
- Ferguson, G., Glidewell, C., Gregson, R. M. & Meehan, P. R. (1998b). *Acta Cryst.* **B54**, 139–150.
- Ferguson, G., Glidewell, C., Gregson, R. M., Meehan, P. R. & Patterson, I. L. J. (1998). *Acta Cryst.* **B54**, 151–161.
- Fredericks, R. J., Doyne, T. H. & Sprague, R. S. (1966). *J. Polym. Sci. Polym. Phys. Ed.* **4**, 899.
- Grell, J., Bernstein, J. & Tinhofer, G. (1999). *Acta Cryst.* **B55**, 1030–1043.
- Harada, Y. & Iitaka, Y. (1974). *Acta Cryst.* **B30**, 1452–1459.
- Harada, Y. & Iitaka, Y. (1977). *Acta Cryst.* **B33**, 247–249.
- Harkema, S. & Gaymans, R. J. (1977). *Acta Cryst.* **B33**, 3609–3611.
- Harkema, S., Gaymans, R. J. & van Hummel, G. J. (1983). *Acta Cryst.* **C39**, 385–387.
- Jeffrey, G. A. (1997). *An Introduction to Hydrogen Bonding*. New York: Oxford University Press.
- Jeffrey, G. A. & Saenger, W. (1991). *Hydrogen Bonding in Biological Structures*. Berlin: Springer-Verlag.
- Jeffrey, G. A. & Takagi, S. (1978). *Acc. Chem. Res.* **11**, 264–270.
- Kinoshita, Y. (1959). *Makromol. Chem.* **33**, 21–31.
- Kubicki, M., Kindopp, T. W., Capparelli, M. V. & Coddling, P. W. (1996). *Acta Cryst.* **B52**, 487–499.
- Kuleshova, L. N. & Zorkii, P. M. (1980). *Acta Cryst.* **B36**, 2113–2115.
- Leiserowitz, L. (1976). *Acta Cryst.* **B32**, 775–802.
- Leiserowitz, L. & Schmidt, G. M. J. (1969). *J. Chem. Soc. A*, pp. 2372–2382.
- Leiserowitz, L. & Tuval, M. (1978). *Acta Cryst.* **B34**, 1230–1247.
- Loehlin, J. H., Franz, K. J., Gist, L. & Moore, R. H. (1998). *Acta Cryst.* **B54**, 695–704.
- Mooij, W. T. M., van Eijck, B. P., Price, S. L., Verwer, P. & Kroon, J. (1998). *J. Comput. Chem.* **19**, 459–474.
- Motherwell, W. D. S. (1999). *Nova Acta Leopoldina*, **79**, 89–98.
- Motherwell, W. D. S., Shields, G. P. & Allen, F. H. (1999). *Acta Cryst.* **B55**, 1044–1056.
- Motherwell, W. D. S., Shields, G. P. & Allen, F. H. (2000). *Acta Cryst.* **B56**, 466–473.
- Nangia, A. & Desiraju, G. R. (1998). *Acta Cryst.* **A54**, 934–944.
- Northolt, M. G. (1974). *Eur. Polym. J.* **10**, 799–804.
- Ota, T., Yamashita, M., Yoshizaki, O. & Nagai, E. (1966). *J. Polym. Sci. Polym. Phys. Ed.* **4**, 959–974.
- Palmer, A. & Brisse, F. (1980). *Acta Cryst.* **B36**, 1447–1452.
- Pauling, L. & Corey, R. B. (1951). *Proc. Natl. Acad. Sci. USA*, **37**, 729–740.
- Pauling, L. & Corey, R. B. (1953). *Proc. Natl. Acad. Sci. USA*, **39**, 253–256.
- Pauling, L., Corey, R. B. & Branson, H. R. (1951). *Proc. Natl. Acad. Sci. USA*, **37**, 205–211.
- Pineault, C. & Brisse, F. (1983a). *Acta Cryst.* **C39**, 1434–1437.
- Pineault, C. & Brisse, F. (1983b). *Acta Cryst.* **C39**, 1437–1439.
- Price, S. L. & Wibley, K. S. (1997). *J. Phys. Chem. A*, **101**, 2198–2206.
- Shintani, R. (1960). *Acta Cryst.* **13**, 609–618.
- Verdonk, M. L., Cole, J. C. & Taylor, R. (1999). *J. Mol. Biol.* **289**, 1093–1108.
- Wells, A. F. (1954). *Acta Cryst.* **7**, 842–848.
- Zorkii, P. M. & Kuleshova, L. N. (1980). *Zh. Strukt. Khim.* **22**, 153–156.