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A Structural Study of Tautomerism and Hydrogen-Bonding in Supramolecular Assemblies

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The synthesis and X-ray structures of four new crystalline materials incorporating 'dimers' assembled from two different units possessing complementary hydrogen bonding motifs are reported; namely, phthalimide and 3-iminoisoindolinone or 2-guanidinobenzimidazole (or selected methylated derivatives) and 2-guanidinobenzoxazole. The bonding within each dimer involves a triplet of hydrogen bonds. The extended supramolecular structures are compared with each other as well as with two related structures described previously. The effect of using complementary DAD/ADA motifs that are not symmetrical on the respective supramolecular structures is also examined as is the prospect of incorporating different tautomeric components into the supramolecular structures. The presence of a very short, proton-transferred hydrogen bond within the respective triplets is also discussed.

Keywords: Crystal engineering; Self-assembly; Supramolecular; Hydrogen bonding

INTRODUCTION

There has been a growing interest in the rational design of crystals containing transition metal complexes that are present as coordination polymers or in which hydrogen bonding and other interactions exist between coordinated ligands [1,2]. In a series of papers [3–7], we have described the formation of molecular assemblies involving metal complexes that incorporate hydrogen bonding triplet motifs in their backbone structure. The resulting supramolecular products have been formed from a metal complex alone, a metal complex together with an organic species, or from two non-equivalent metal complexes (all possessing complementary triplet hydrogen bonding motifs).

One of the ligands of interest was *N″*-1*H*-benzimidazol-2-ylguanidine (2-guanidinobenzimidazole, gbH) which itself contains a donor–acceptor–donor (DAD) hydrogen bonding motif that is not involved in metal binding when the anionic form of the ligand forms a metal complex. Further, the neutral bis-ligand nickel(II) complex has been observed to occur in different tautomeric forms so that the complex may possess either a DAD motif (identical with the free ligand) or a DDA motif [3,8]. Similarly, in the case of the related ligand *N″*-(5,6-dimethyl-1H-benzimidazol-2-yl)guanidine, Me_2gbH, the neutral bis-ligand nickel(II) complex was observed to occur in two tautomeric forms in the same crystal [6].

Organic bases such as phthalimide and 1,8-naphthalimide, incorporating symmetrical potential ADA hydrogen bonding motifs, have been demonstrated to form adducts with transition metal complexes that have complementary, symmetrical DAD motifs [5,9]. It is noted that even though both oxygen acceptors in the triplets may be equivalent in the isolated adducts, they may become non-equivalent when those adducts link to form more extended structures. For instance, one of the oxygen atoms may act as an acceptor for two hydrogen bonds and the other only one. In these circumstances it has proved possible to use a less symmetrical building block, 3-iminoisoindolinone, in which an oxygen atom in phthalimide has been replaced by an

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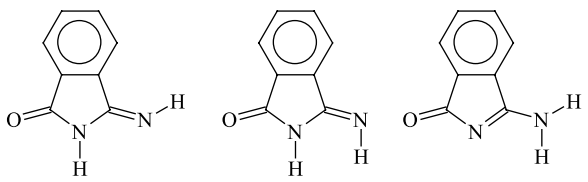
NH group, to build an equivalent supramolecular structure [5]. Whether this is feasible when the DAD motif is not symmetrical, as in the case of gbH, is a question addressed in this study. Also of interest when employing complementary motifs is the possibility that different tautomeric forms of the intended building blocks might occur; one such system in which the forms are close together in energy is 3-iminoisoindolinone (Scheme 1).

A computational study of the tautomers of 3-iminoisoindolinone [10] has shown that tautomer **I** is the most stable, but that **II** is just 3.9 kJ mol^{-1} less stable (in good agreement with 3.6 kJ mol^{-1} obtained from an NMR study) [11] while **III** is calculated to be 12.9 kJ mol^{-1} less stable than **I**. This may be compared with the pattern for phthalimide, for which the diketo tautomer is expected to predominate over the hydroxy-keto form. It was the *E* tautomer, with its ADA motif, that was observed in the adduct with bis(dithiobiureto)nickel(II) [5]. Whether the energy difference between **I** and **II** is small enough to allow incorporation of **II** in an adduct by providing a DAA template rather than a DAD one is a second question addressed in this study. In this context it is noted that *N″*-1,3-benzoxazol-2-ylguanidine (2-guanidinobenzoxazole, goH), in which an oxygen atom replaces a nitrogen atom in the benzimidazole ring system, is relatively straightforward to prepare [12] and does provide the required DAA motif in a molecule similar to gbH.

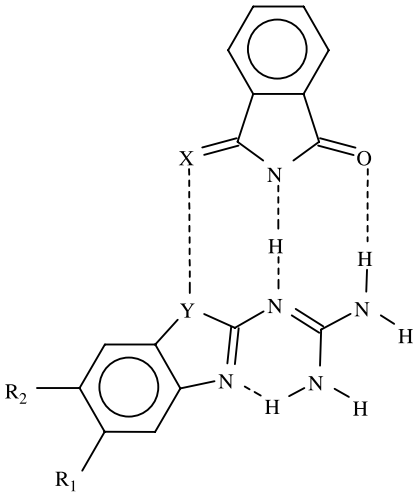
In the course of our earlier investigations of supramolecular systems based on gbH, we observed that when gbH and phthalimide form a 1:1 adduct involving their complementary hydrogen binding motifs, the central hydrogen bond in the triplet is a 'proton transferred' hydrogen bond and was found to be unusually short [7]. Such proton transfer was not observed in the phthalimide adducts with transition metal complexes [4] or in the adduct formed between phthalimide and Me_2gbH [6]. Of course, in the latter case the additional methyl groups change both the pKa and the steric requirements of the molecule and it is hence no surprise that the supramolecular structure is quite different.

In an extension of the above studies, an investigation of new hydrogen bonded triplet assemblies, restricted to systems in which only organic components are present (see Scheme 2), is now reported.



I II III

SCHEME 1



	X	Y	R_1	R_2
1[a]	O	NH	Me	Me
2	*E*–NH	NH	Me	Me
3	*E*–NH	NH	H	H
4[b]	O	NH	H	H
5	O	NH	H	Me
6	*Z*–NH	O	H	H

SCHEME 2 [a]Ref. [6]. [b]Ref. [7].

EXPERIMENTAL

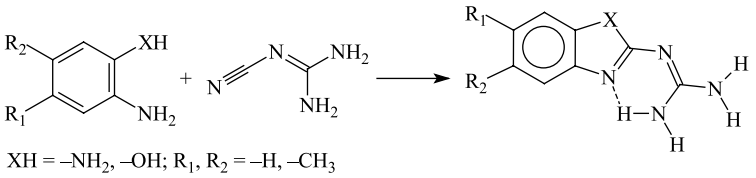
Synthesis

N″-1*H*-benzimidazol-2-ylguanidine (2-guanidinobenzimidazole), phthalimide, 3-iminoisoindolinone, 2-aminophenol and 2-amino-4,5-dimethylphenylamine (4,5-dimethyl-1,2-phenylenediamine)were purchased commercially and used without further purification. 2-Amino-4-methylphenylamine (3,4-diaminotoluene) was also purchased commercially but recrystallised from 60/80 petroleum ether before use.

N″-1,3-benzoxazol-2-ylguanidine, *N″*-(5,6-dimethyl-1H-benzimidazol-2-yl)guanidine and *N″*-(6-methyl-1H-benzimidazol-2-yl)guanidine were prepared by literature methods (Scheme 3) [12,13].

General Method for Preparation of the Hydrogen Bonded Adducts

Crystals of the hydrogen bonded adducts suitable for X-ray diffraction were obtained by dissolving



SCHEME 3

1 mmol of both components in absolute ethanol (10 mL) and allowing the solvent to evaporate slowly. In the case of *N‴*-1,3-benzoxazol-2-ylguanidine: (3Z)-3-iminoisoindolinone, **6**, the evaporation was very slow and the crystals that formed consisted of a mixture of the required adduct with some contamination from the starting materials. While a single crystal suitable for X-ray determination was able to be selected, in view of the above, a bulk sample was not submitted for microanalysis.

[N‴-(5,6-dimethyl-1H-benzimidazol-2-yl)guanidine: (3E)-3-iminoisoindolinone], 2

Anal. Calcd. for $C_{18}H_{19}N_7O$ (%): C, 61.88; H, 5.48; N, 28.06. Found: C, 62.16; H, 5.53; N, 28.14.

[N‴-1H-benzimidazol-2-ylguanidine: (3E)-3-iminoisoinolinone], 3

Anal. Calcd. for $C_{16}H_{15}N_7O$ (%): C, 59.80; H, 4.70; N, 30.51. Found: C, 59.33; H, 4.54; N, 29.40.

[N‴-(6-methyl-1H-benzimidazol-2-yl)guanidine: Phthalimide], 5

Anal. Calcd. for $C_{17}H_{16}N_6O_2$ (%): C, 60.71; H, 4.79; N, 24.99. Found: C, 60.69; H, 4.78; N, 24.77.

X-ray Crystal Structure Determination

Data for the crystal structures of **2** and **5** were collected at 150K on a Bruker SMART 1000 CCD diffractometer with an Oxford Cryosystems Cryostream [14], using graphite monochromated MoKα radiation (0.71073 Å) from a sealed tube. Data were integrated using SAINT [15] and a Gaussian absorption correction [15,16] was applied to the data. Subsequent computations were carried out with the WinGX [17] and XTAL [18] graphical user interfaces.

Data for structures **3** and **6** were collected on a Bruker-Nonius Kappa CCD area detector diffractometer at 150 K using MoKα radiation produced by a Bruker-Nonius FR591 rotating anode generator (l = 0.71073A). Data collection strategies and initial cell refinement were carried out using DENZO [19], and COLLECT [20].

The structures were solved by direct methods [21] and refined by full-matrix least-squares using the SHELX-97 [22] suite of programs. Data were corrected for the effects of absorption by comparison of equivalent reflections using the program SORTAV [23] Final refinement data are listed in Table I, and details of hydrogen bond geometry are given in Tables II and III. Ortep [24] depictions are shown in Figs. 1–4. The non-hydrogen atoms were modelled with anisotropic displacement parameters, and a riding atom model was used for the hydrogen atoms (with the exception of the amine hydrogens) with each H atom having U_{eq} 1.5 times that of the parent atom U_{iso}. Amine hydrogen sites were located from a difference Fourier map, and freely refined with isotropic displacement parameters. In the refinement of **5** significant residual electron density remained and this is attributed to unresolved disorder; there is no evidence for twinning.

CIF files for all structures are deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 274116–274119.

RESULTS AND DISCUSSION

The potential hydrogen bonding triplet motif on Me_2gbH is not symmetrical; one of the donors, D(im), is an imidazole NH group and the other, D(g), is a guanidine NH.

The complementary ADA motif on phthalimide, however, is symmetrical, so that there is only one way in which the hydrogen bond triplet can be formed between the two motifs. The [Me_2 gbH:phthalimide] dimers so formed are linked into ribbons (Scheme 4) by hydrogen bonds formed between a guanidine NH donor and a phthalimide O acceptor in neighbouring dimers. It is the phthalimide O joined to D(im) in the triplet that accepts a second hydrogen bond; the oxygen atom joined to D(g) is only involved in the triplet [6].

The ribbon formation observed in the above case resembles that found when bemegride (3-ethyl-3-methylglutarimide) forms a 2:1 hydrogen bonded complex with bis(dithiobiureto)nickel(II) [9]. Only one of the two imide oxygens accepts two hydrogen bonds.

TABLE I X-ray crystal data for **2**, **3**, **5** and **6**

	2	**3**	**5**	**6**
Formula of the Refinement Model	$C_{18}H_{19}N_7O$	$C_{16}H_{15}N_7O$	$C_{17}H_{16}N_6O_2$	$C_{16}H_{14}N_6O_2$
Model Molecular Weight	349.40	321.35	336.36	322.33
Crystal System	Monoclinic	Monoclinic	Monoclinic	monoclinic
Space Group	$P2_1/c$(14)	$P2_1/c$(14)	$P2_1/n$(14)	$P2_1/c$(14)
A	14.778(3) Å	13.2843(4) Å	12.202(3) Å	13.2056(3) Å
B	7.1360(14) Å	7.1210(2) Å	8.4350(18) Å	7.1026(2) Å
C	16.236(3) Å	15.8271(6) Å	16.624(4) Å	16.8298(4) Å
β	98.867(4)°	95.6010(10)°	110.861(3)°	107.9020(10)°
V	1691.7(6) $Å^3$	1490.06(8) $Å^3$	1598.9(6) $Å^3$	1502.11(7) $Å^3$
D_c	1.372 g cm^{-3}	1.432 g cm^{-3}	1.397 g cm^{-3}	1.425 g cm^{-3}
Z	4	4	4	4
Crystal Size	0.498 × 0.175 × 0.047 mm	0.5 × 0.1 × 0.02 mm	0.510 × 0.490 × 0.462 mm	0.4x0.22x0.04 mm
Crystal Colour	Yellow	Brown	Yellow	colourless
Crystal Habit	Blade	Blade	Prism	plate
Temperature	150(2) Kelvin	120 K	150(2) Kelvin	120 K
λ(MoKα)	0.71073 Å	0.71073 Å	0.71073 Å	0.71073 Å
μ(MoKα)	0.092 mm^{-1}	0.144 mm^{-1}	0.097 mm^{-1}	0.100 mm^{-1}
$T(\text{Gaussian})_{min,max}$	0.965, 0.997	1.077, 0.946	0.944, 0.966	1.064, 0.861
$2\theta_{max}$	52.84°	54.96°	55.92°	54.96°
hkl range	−18 18, −8 8, −20 20	−15, 17, −8, 9, −19, 20	−15 14, −11 11, −21 21	−1714, −98, −21 21
N	16751	13562	14335	12702
N_{ind}	3470(R_m0.0816)	3363 ($R_m = 0.062$)	3574(R_m0.0227)	3419 ($R_m = 0.077$)
N_{obs}	2335(I > 2σ(I))	2630	2896(I > 2σ(I))	2667
N_{var}	265	240	251	241
Residuals* *R*1(*F*), *wR*2(F^2, all data)	0.0359, 0.0839	0.0435, 0.1069	0.0622, 0.1400	0.0432, 0.1202
GoF(all)	1.190	1.039	1.264	1.025
Residual Extrema	−0.201, 0.172 e^- $Å^{-3}$	−0.17, 0.26	−0.354, 1.233 e^- $Å^{-3}$	−0.37, 0.27

For **2**, $w = 1/[\sigma^2(F_0^2) + (0.03P)^2]$ where $P = (F_0^2 + 2F_c^2)/3$; for **3**, $w = 1/[\sigma^2(F_0^2) + (0.0466P)^2 + 0.4991P]$ where $P = (F_0^2 + 2F_c^2)/3$; for **5**, $w = 1/[\sigma^2(F_0^2) + (0.03P)^2 + 1.5P]$ where $P = (F_0^2 + 2F_c^2)/3$; for **6**, $w = 1/[\sigma^2(F_0^2) + (0.0678P)^2 + 0.2697P]$ where $P = (F_0^2 + 2F_c^2)/3$.* $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ for $F_0 > 2\sigma(F_o)$; $wR2 = (\Sigma w(F_0^2 - F_c^2)^2/\Sigma(wF_c^2)^2)^{1/2}$ all reflections.

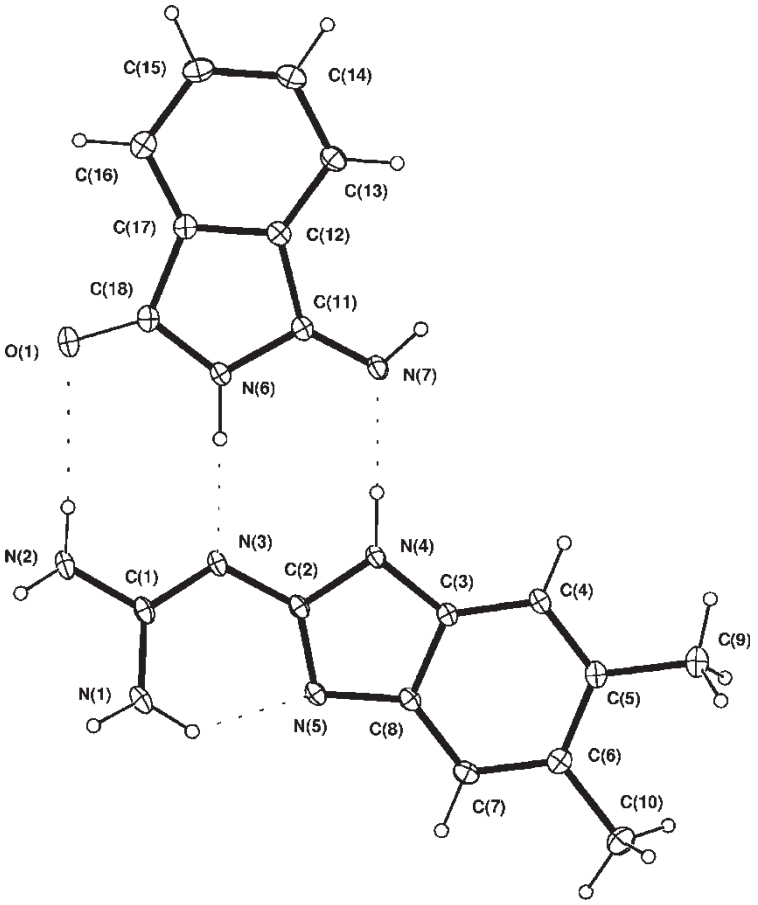


FIGURE 1 An Ortep [23] depiction of **2** with displacement ellipsoids at the 20% level.

3-Iminoisoindolinone resembles phthalimide but has an unsymmetrical ADA motif. One acceptor is an oxygen atom, A(O), and is capable of acting as an acceptor for a second hydrogen bond; the other acceptor is an imino nitrogen, A(NH), which can act as a donor for a second hydrogen bond, but not an acceptor. Thus, there are two ways in which the complementary triplet could be formed between Me_2gbH and 3-iminoisoindolinone (Scheme 5). A(O) may form a hydrogen bond with D(g), as in **IV**, or with D(im), as in **V**.

Bis(dithiobiureto)nickel(II) has a symmetrical DAD motif on each ligand and we have shown that two molecules of (3E)-3-iminoisoindolinone bind to the complex to form a centrosymmetric adduct. In this case the extended supramolecular structure remains the same as that formed by the phthalimide adduct, with the 3-iminoisoindolinone orienting itself so that the carbonyl occupies the position in which the bridging hydrogen bond is formed and the imino group, which can accept only one hydrogen bond, occupies the other.

The complex obtained on interaction of Me_2gbH and 3-iminoisoindolinone, **2**, has complementary DAD/ADA hydrogen bonding motifs paired so that dimers linked by a hydrogen bond triplet are formed. The central hydrogen bond is slightly longer than that observed for phthalimide in **1**, but the NH...O hydrogen bond in the triplet is very long (Table II). 3-Iminoisoindolinone is present as the E-tautomer (**I**) and its orientation is that shown in **IV**, in which D(g) is paired up with A(O) and D(im) with A(NH).

The N(1), C(1), N(2) and N(3) atoms of Me_2gbH are co-planar (rms deviation from plane 0.009 Å) but the plane is twisted with respect to the imidazole plane by 18.68(06)°; the torsion angle C(1)–N(3)–C(2)–N(5) is −18.49(0.22)°. This geometry more closely resembles that of 'free' Me_2gbH than that for **1**, in which the guanidino group is twisted so that it is almost in the same plane as the benzimidazole residue and the corresponding torsion angle is only −6.18(17)° [5].

The isoindoline plane is almost parallel to that of the benzimidazole, making an angle of just 1.66(0.04)° with it. As a result, of the two $R_2^2(8)$rings that make up the triplet, one, N(3)–C(2)–N(4)–N(7)–C(11)–N(6), is planar (rms deviation from the plane 0.005 Å) and the other, N(3)–C(1)–N(2)–O(1)–C(18)–N(6), is not (rms deviation from the plane 0.09 Å). The $R_2^2(8)$rings yield an angle of 6.12(0.05)° with each other.

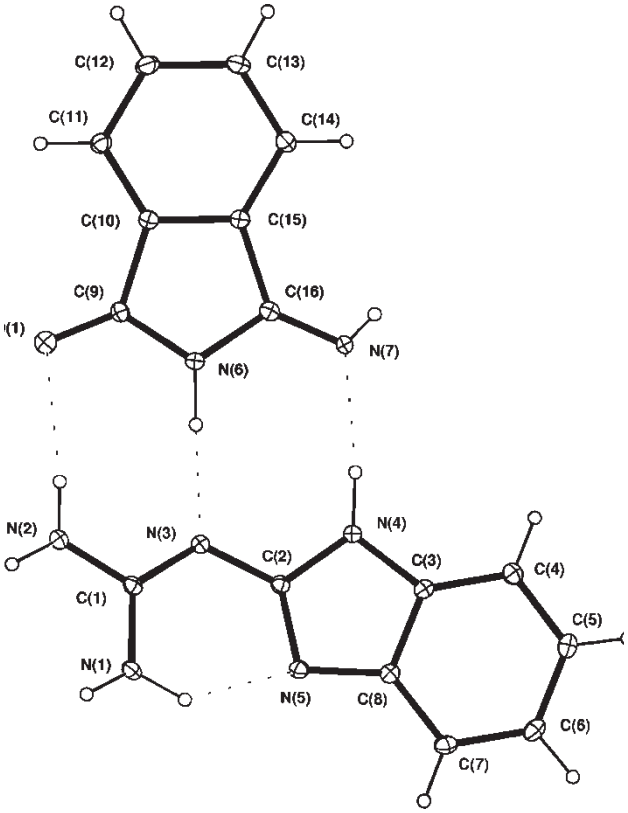


FIGURE 2 An Ortep [24] depiction of **3** with displacement ellipsoids at the 20% level.

The orientation of the (3E)-3-iminoisoindolinone in the dimers means that the extended ribbons observed in **1** are not possible in this case. Instead, the dimers are joined by long hydrogen bonds between guanidino NH donors (N(1) and N(2), not involved in the triplet or the intramolecular hydrogen bond) and the π electron densities of N(3) and N(5) respectively. The zig-zag chains so formed are shown in Fig. 5 and run quasi-parallel to the *b* axis. There is no close stacking of the aromatic residues, the planes of which are separated by approximately 3.4 Å.

The structure of the adduct [gbH:3-iminoisoindolinone], **3**, differs only in detail from that of **2** described above. The crystal is denser than that of **2**, presumably as a result of the absence of the methyl groups, which otherwise have little effect on the supramolecular assembly; the crystals containing methyl-substituted benzimidazoles are all less dense than the other structures.

The N(1), C(1), N(2) and N(3) atoms of the gbH guanidino group are co-planar (rms deviation from plane 0.008 Å) but the plane is twisted with respect to the imidazole plane by 15.60(0.06)°; the C(1)–N(3)–C(2)–N(5) torsion angle is −18.49(0.22)°.

The isoindoline plane is almost parallel to that of the benzimidazole, making an angle of just 4.26(0.03)° with it. As a result, of the two $R_2^2(8)$rings

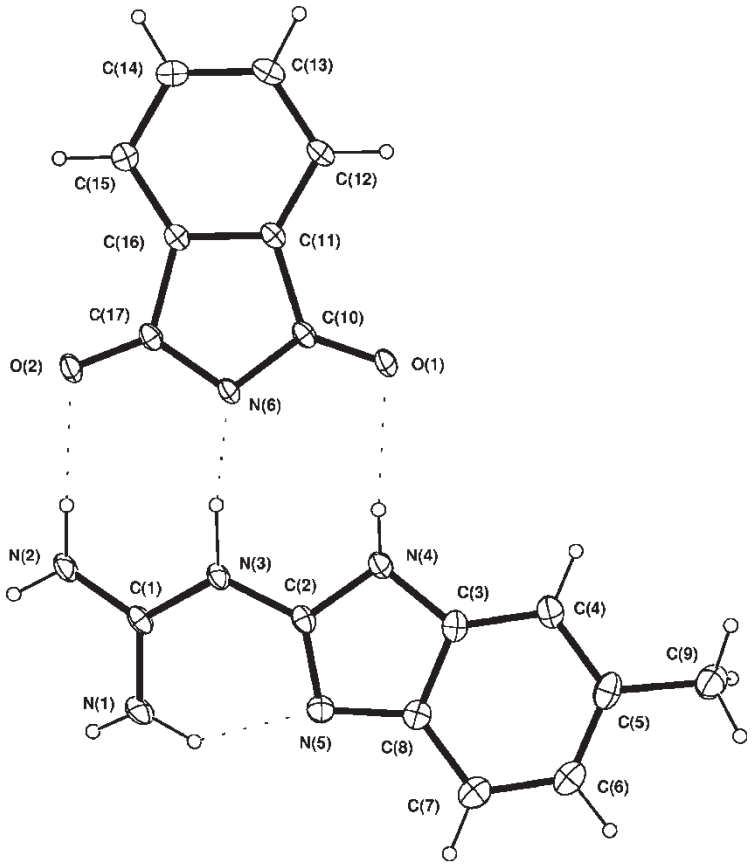


FIGURE 3 An Ortep [24] depiction of **5** with displacement ellipsoids at the 20% level.

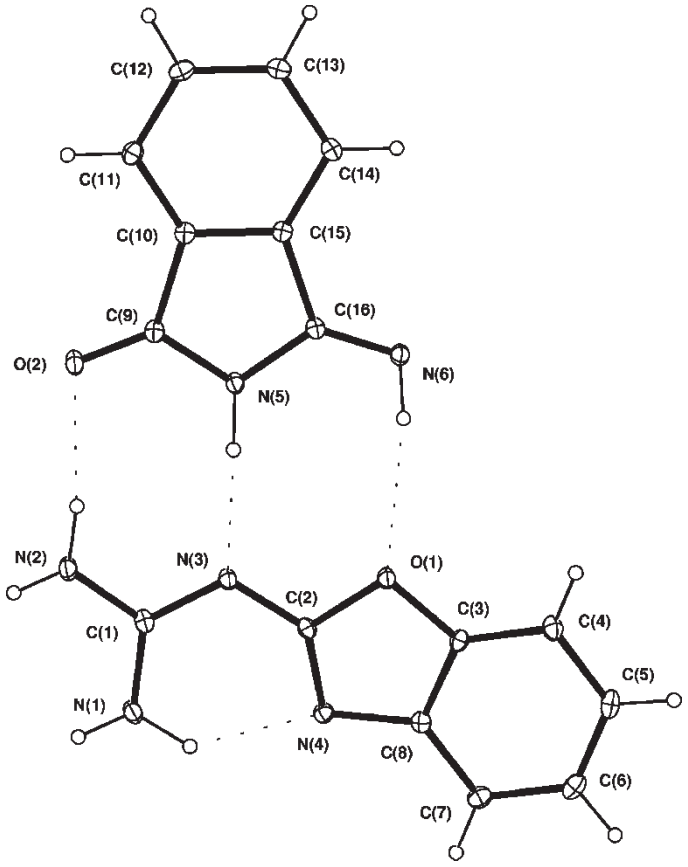
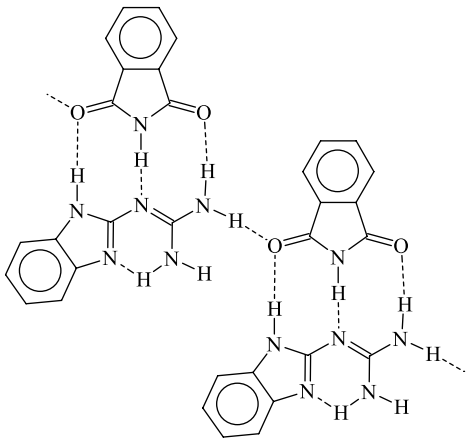


FIGURE 4 An Ortep [23] depiction of **6** with displacement ellipsoids at the 20% level.

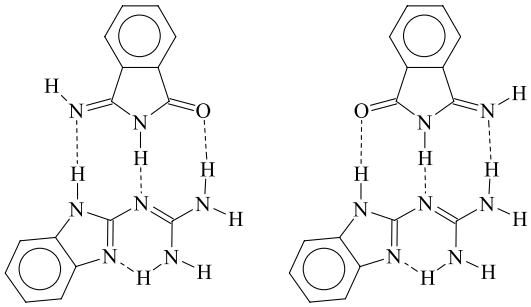
that make up the triplet, one, N(3)–C(2)–N(4)–N(7)–C(11)–N(6), is planar (rms deviation from the plane, 0.016 Å) and the other, N(3)–C(1)–N(2)–O(1)–C(18)–N(6), is not (rms deviation from the plane 0.13 Å). The $R_2^2(8)$rings make an angle of 8.40(0.05)° with each other. The central hydrogen bond is approximately the same length as that in **2** and the NH···O hydrogen bond in the triplet is still rather long, but is shorter than that in **2** (Table II).

As in **2**, the dimers are joined by long hydrogen bonds between guanidino NH donors, N(1) and N(2), and the π electron density on N(3) and N(5) respectively.

The structure of [gbH:phthalimide], **4**, is very different from that of **1** [6]. The two components form dimers with a hydrogen bonded triplet and all three bonds in the triplet in **4** are shorter than the corresponding bonds in **1**. The central hydrogen bond is particularly short and is, in fact, a proton transferred hydrogen bond. This means that the triplet is a combination of DDD and AAA motifs rather than the expected DAD–ADA arrangement. All secondary interactions are attractive in AAA-DDD assemblies and increase the stability of the triplet, whereas there is a net destabilising effect of



SCHEME 4



SCHEME 5

TABLE II A summary of the hydrogen bond lengths in the complementary triplets (see also Scheme 1)

	d(XY)/Å	d(NN)/Å	d(NO)/Å
1 [5]	3.0602(15)	2.7656(16)	3.0239(17)
2	2.8469(19)	2.8600(18)	3.320(2)
3	2.9113(18)	2.8204(17)	3.1572(18)
4[a] [6]	2.929(4)	2.6821(18)	2.963(5)
4 [6]	2.9353(19)	2.692(4)	2.960(2)
5	2.917(3)	2.682(3)	2.954(3)
6	3.2069(16)	2.8400(17)	2.9926(17)

[a] Neutron diffraction data

2–3 kcal/mol in ADA–DAD triplets [25]. The crystal packing differs markedly from that in **1**, which may be, at least in part, due to the formal charges generated by the proton transfer.

N^{II}-(6-methyl-1H-benzimidazol-2-yl)guanidine, MegbH, forms the adduct [MegbH:phthalimide], **5**, with phthalimide. The supramolecular structure of **5** (Fig. 6) resembles that of **4** rather than that of **1**. The central hydrogen bond in the hydrogen bond triplet in the dimers is very short, 2.682(3) Å, and is a proton transferred hydrogen bond. Like **4**, but unlike **1**, the hydrogen bond formed by D(im) is slightly shorter than that involving D(g) (see Tables II and III). All hydrogen bond donor and acceptor sites are utilised in building the supramolecular structure (Fig. 7) so that, apart from the triplet, both phthalimide oxygen atoms accept a second hydrogen bond from guanidine N(1) and N(2) donors.

The dimers stack in columns parallel to the *b* axis of the unit cell; adjacent layers within a column are related by inversion and are separated by approximately 3.3 Å. Neighbouring glide related columns of dimers are linked to one another through hydrogen bonding between donor N(1) and acceptor O(2) atoms on glide related molecules, and between donor N(2) and acceptor O(1) on another glide related molecule (Table III). The nitrogen atoms that form the central hydrogen bond of the triplet are offset from the centre of the π electron system of a phthalimide molecule in an adjacent layer; they are aligned with the ring centroids in **1**. This slight change in orientation may be a result of the steric requirements of the methyl group.

TABLE III Hydrogen bond geometry

(a) Complex **2**

Donor	Hydrogen	Acceptor		D-H(Å)	H-A(Å)	D-A(Å)	DHA Angle(°)
N(2)	H(2NA)	O(1)		0.877(18)	2.451(18)	3.320(2)	171.1(15)
N(4)	H(4N)	N(7)		0.967(16)	1.880(17)	2.8469(19)	178.4(14)
N(6)	H(6N)	N(3)		0.975(18)	1.885(19)	2.8600(18)	179.2(16)
N(1)	H(1NA)	N(5)		0.901(18)	2.037(19)	2.709(2)	130.4(15)
N(2)	H(2NB)	N(5)[a]	2_554	0.905(19)	2.210(19)	3.080(2)	160.8(15)
N(1)	H(1NB)	N(3)[a]	2_554	0.834(19)	2.53(2)	3.2977(19)	152.9(16)

(b) Complex **3**

Hydrogen bonds with H..A < r(A) + 2.000 Angstroms and < DHA > 110 deg.

D-H	d(D-H)	d(H..A)	< DHA	d(D..A)	A
N2–H2NA	0.903	2.265	169.45	3.157	O1
N4–H4N	0.952	1.965	172.22	2.911	N7
N6–H6N	0.977	1.844	178.51	2.820	N3
N1–H1NA	0.931	1.993	133.59	2.720	N5
N1–H1NB	0.904	2.395	165.99	3.280	N3[b]
N2–H2NB	0.912	2.165	178.63	3.077	N5[b]

(c) Complex **5**

Donor	Hydrogen	Acceptor	D-H(Å)	H-A(Å)	D-A(Å)	DHA Angle(°)
N(4)	H(4N)	O(1)	0.80(2)	2.12(2)	2.917(3)	175(2)
N(2)	H(2NA)	O(2)	0.92(3)	2.04(3)	2.954(3)	179(3)
N(3)	H(3N)	N(6)	1.01(3)	1.68(3)	2.682(3)	172(3)
N(1)	H(1NA)	N(5)	0.91(3)	1.99(3)	2.716(3)	135(3)
N(2)	H(2NB)	O(1)[c]	0.86(3)	2.03(3)	2.884(3)	175(3)
N(1)	H(1NB)	O(2)[d]	0.86(3)	2.05(3)	2.822(3)	148(3)

(d) Complex **6**

Hydrogen bonds with H..A < r(A) + 2.000 Angstroms and < DHA > 110 deg.

D-H	d(D-H)	d(H..A)	< DHA	d(D..A)	A
N2–H2NA	0.917	2.083	171.26	2.993	O2
N6–H6N	0.914	2.303	170.18	3.207	O1
N5–H5N	0.965	1.875	178.82	2.840	N3
N1–H1NA	0.952	1.970	135.24	2.729	N4
N1–H1NB	0.865	2.184	156.91	2.999	O2[e]
N2–H2NB	0.887	2.037	169.41	2.913	N6[f]

[a] −x, y + 1/2, −z − 1/2; [b] −x + 1, y − 1/2, −z + 1/2; [c] x − 1/2, 1/2 − y, z − 1/2; [d] −x + 1/2, y − 1/2, −z − 1/2; [e] −x, y − 1/2, −z + 1/2; [f] x, −y + 1/2, z + 1/2

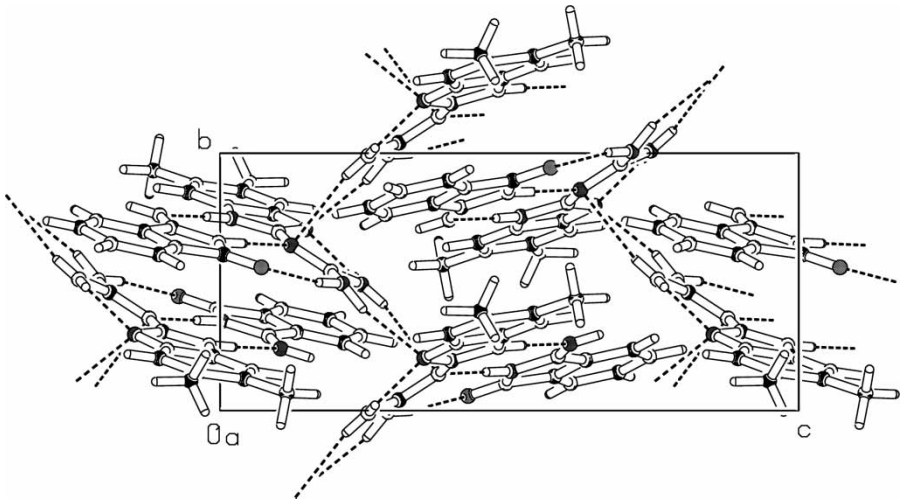


FIGURE 5 A Platon [25,26] depiction of the unit cell of **2** viewed along the *a* axis.

The atoms of the gbH guanidino group N(1), C(1), N(2) and N(3) are co-planar (rms deviation from plane, 0.0007 Å) but the plane, is twisted with respect to the imidazole plane by 14.37(0.14)°; the C(1)–N(3)–C(2)–N(5) torsion angle is −14.65(0.37)°. The planes of the phthalimide and the imidazole ring systems make an angle of just 4.84(0.09)° with each other and the angle between the guanidino group and the phthalimide plane is 11.13(0.14)°. That is, the aromatic ring systems are approximately co-planar and the guanidine is twisted out of this plane.

Of the two $R_2^2(8)$rings that make up the triplet, one, N(3)–C(2)–N(4)–O(1)–C(10)–N(6), is planar (rms deviation from the plane, 0.0212 Å) and makes an angle with the phthalimide ring system of just 0.27(0.10)° and the other, N(3)–C(1)–N(2)–O(2)–C(17)–N(6), is less so (rms deviation from the plane, 0.0901 Å). The $R_2^2(8)$rings make an angle of 6.97(0.10)° with each other.

2-Guanidinobenzoxazole is similar in size and shape to 2-guanidinobenzimidazole but the potential hydrogen bonding motif is DAA rather than DAD. This means that the complementary motif required to form a hydrogen bonded triplet is ADD and the *Z* tautomer of 3-iminoisoindolinone, **II**, has just such a motif. The system has the potential to form the same extended supramolecular structure as observed in **4** and **5**, but there are differences. The *Z* tautomer is less stable than the *E* tautomer (which has been observed in all the other assemblies, the secondary repulsions associated with the DAA/ADD triplet are more favourable than those associated with

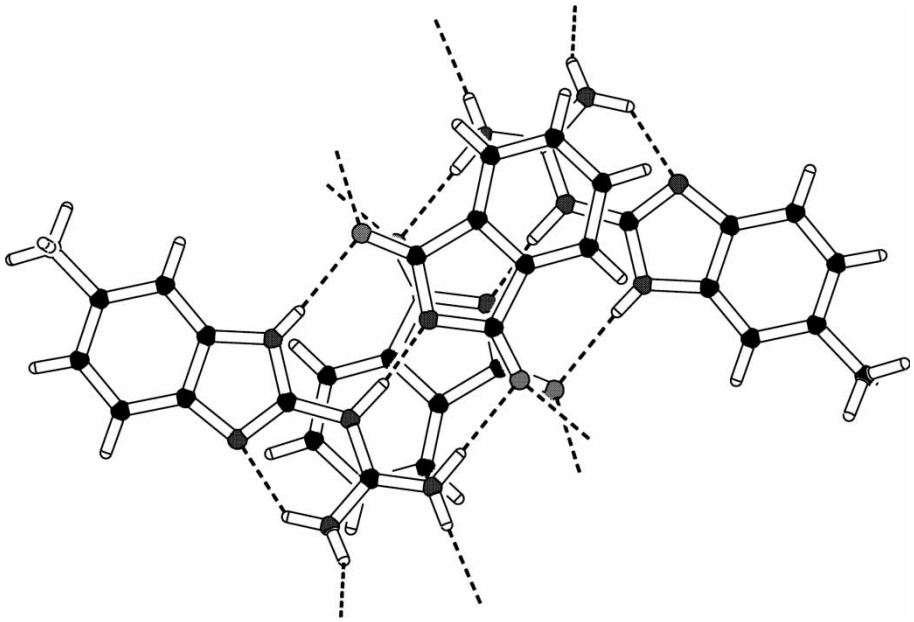


FIGURE 6 A Platon [26,27] depiction of the stacking of two dimers in **5**, showing the alignment of the central hydrogen bond and the imidazole ring system.

DAD/ADA and less favourable than for AAA/DDD, and the strength of the hydrogen bond between the imino NH donor and the oxazole oxygen atom may all affect the outcome.

The X-ray diffraction study of **6** shows that 2-guanidinobenzoxazole and (3Z)-3-iminoisoindolinone do form a 1:1 adduct that has a hydrogen bonded triplet within the dimers and approximately the same extended supramolecular structure as observed in **4** and **5**.

The central hydrogen bond in the hydrogen bond triplet within the dimers is no longer very short, nor is it a proton transferred hydrogen bond, but has approximately the same length as those formed by the *E* tautomer in **2** and **3**. Also, the hydrogen bond formed by the D(g) is now the shorter of the two other bonds in the triplet and the hydrogen bond between the oxazole oxygen (acceptor) and the imino NH (donor) is very long for a NH···O hydrogen bond (Tables II and III). Both the isoindolinone substituents, the carbonyl oxygen atom and imino nitrogen atom, accept second hydrogen bonds from guanidine N(1) and N(2) donors to form the extended supramolecular structure.

The dimers stack in columns parallel to the *b* axis of the unit cell; adjacent layers within a column are related by inversion and are separated by approximately 3.3 Å. Neighbouring glide related columns of dimers are linked to one another through hydrogen bonding between donor N(1) and acceptor O(2) atoms on glide related molecules, and between donor N(2) and acceptor N(6) on another glide related molecule (Table III). The nitrogen atoms that form the central hydrogen bond of the triplet are offset from the centre of the π electron system of a phthalimide molecule in an adjacent layer.

The N(1), C(1), N(2) and N(3) atoms of the gbH guanidino group are co-planar (rms deviation from plane, 0.0003 Å) but the plane is twisted with respect to the imidazole plane by 10.16 (0.05)°; the C(1)–N(3)–C(2)–N(5) torsion angle is 8.56(0.23)°. Unlike **5**, it is the guanidino and isoindoline systems that are approximately co-planar and the benzoxazole ring system is twisted out of this plane. The guanidino and isoindoline planes are inclined at an angle of just 2.54(0.06)° with each other and the angle between the benzoxazole rings and the isoindoline plane is 12.70(0.03)°.

Of the two $R_2^2(8)$rings that make up the triplet, one, N(3)–C(2)–O(1)–N(6)–C(16)–N(5), is less planar (rms deviation from the plane, 0.0783 Å) than the other, N(3)–C(1)–N(2)–O(2)–C(9)–N(5) (rms deviation from the plane, 0.0142 Å). The $R_2^2(8)$ rings make an angle of 2.37(0.03)° with each other.

In all the structures **1–6,** the central hydrogen bond of the triplet always involves the guanidino nitrogen N(3) competing with the nitrogen atom of the isoindole ring system for a proton. The nature of the hydrogen bond, then, would be expected to depend on the proton donor and acceptor abilities of the two nitrogen atoms. It may also depend on the local environment of the bond, which depends on the extended supramolecular structure in the crystal. The tuning of physical properties such as pKa by the local environment is often observed in the active sites of enzymes.

If one compares **2** and **3**, it is clear that whatever the differences that the methyl substituents make to

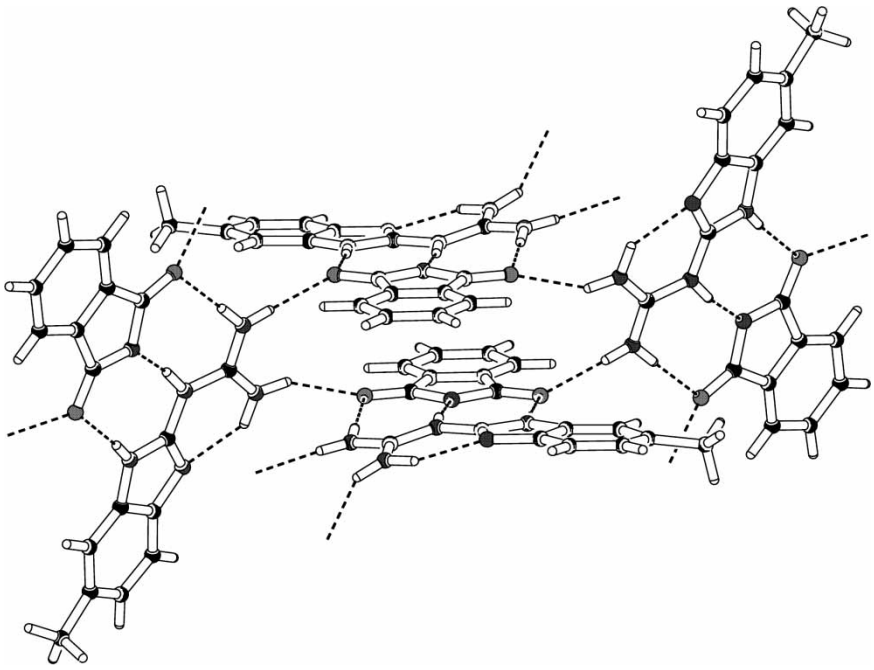


FIGURE 7 A Platon [25,26] depiction of the hydrogen bonding in **5**.

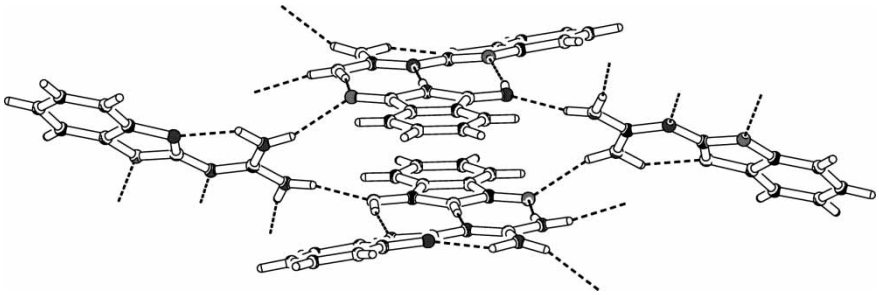


FIGURE 8 A Platon [25,26] depiction of the hydrogen bonding in **6**.

the proton acceptor ability of N(3), the length of the central hydrogen bond is not significantly affected. It would be expected, then, that if **4** and **5** had the same extended supramolecular structure as **1** the central hydrogen bond would be essentially the same length in each.

However, **4** and **5** have a central hydrogen bond that is much shorter than that observed in **1**, and is also a proton transferred hydrogen bond. It seems, then, that the extended supramolecular structure observed in **4** and **5** is somehow involved in the formation of this bond. It could, of course, be possible that this extended structure, in which all the hydrogen bond donors and acceptors are used, is only possible if the central hydrogen bond is a charge transferred hydrogen bond, with the attendant change in pattern of complementary motifs and dipole associated with the dimers.

Crystals of **6** contain the same extended supramolecular structure (Fig. 8 and 9) as **4** and **5**, but the dimers do not contain a triplet in which the central hydrogen bond is a proton transferred bond, and the length of the central bond lies between those observed in **2** and **3**. The energy cost of incorporating the less stable *Z* tautomer in the triplets is expected to be offset to some extent by the more favourable secondary interactions in the complementary motifs. The acceptor abilities of the two nitrogens in the central hydrogen bond in the dimers in **6** are perhaps not sufficiently close, or perhaps the acceptor ability of the benzimidazole oxygen is too low to permit proton transfer in the central hydrogen bond.

On the evidence presented here, then, it would seem that the best explanation for the unusual hydrogen bond behaviour observed in **4** and **5** is that the proton acceptor ability of N(3) is only slightly less than that of N(6) and that the local environment produced as a result of the extended supramolecular structure 'tunes' the system to tip the balance in favour of proton transfer.

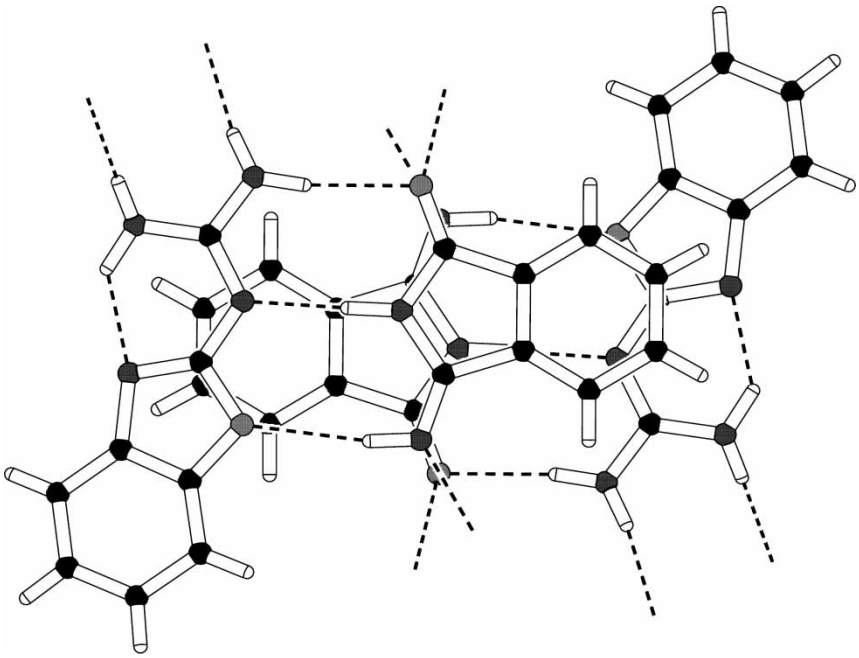


FIGURE 9 A Platon [25,26] depiction of the stacking of the central hydrogen bond of the triplet and the isoindoline rings in **6** viewed perpendicular to the isoindoline system.

CONCLUSIONS

In this study we have compared the supramolecular structures formed by a series of 'organic' dimers bound together by hydrogen bond triplets.

(3E)-3-Iminoisoindolinone can orient itself in two different ways when it forms a triplet of hydrogen bonds with molecules based on 2-guanidinobenzimidazole. It was observed that the isoindolinone carbonyl oxygen preferentially acts as an acceptor for the guanidino NH in the motif rather than the imidazole NH, and this leads to a different extended supramolecular structure from that observed in the more symmetrical phthalimide analogue.

It was also observed that by using a template with a potential hydrogen bonding motif that was DAA rather than DAD, it was possible to grow crystals that incorporated the less stable *Z* tautomer of 3-iminoisoindolinone into a supramolecular array. In the latter all the possible hydrogen bond donors and acceptors are utilised.

By comparing the supramolecular structures observed in this study it would seem that the best rationale for the formation of a proton transferred hydrogen bond is that the proton acceptor and donor abilities of the two molecules involved are similar and that the local environment produced as a result of the extended supramolecular structure formed acts to tip the balance in favour of proton transfer.

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