Crystal Engineering

Multidentate, V-Shaped Pyridine Building Blocks as Tectons for Crystal Engineering

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Abstract: The formation of supramolecular structural units through self-assembly is a powerful method to design new architectures and materials endowed with specific properties. With the aim of adding a group of versatile tectons to the toolkit of crystal engineers, we have devised and synthesised four new V-shaped building blocks characterised by an aryl acetylene scaffold comprising three substituted pyridine rings connected by two triple bonds. The judicious choice of different substituents on the pyridine rings provides these tectons with distinctive steric, electrostatic and

Introduction

Self-assembly is one of the key strategies to generate sophisticated architectures, from discrete cages to 3D networks.^[1] Molecular tectons endowed with functionalities suitable for both metal coordination and weak interactions are interesting building blocks for generating new materials with desired properties.^[2] In this context, multidentate tectons bearing pyridine groups are extremely versatile. Pyridines can interact with metals but are also excellent hydrogen- and halogen-bond acceptors. In addition, their aromaticity promotes π - π stacking, C–H··· π and C–F··· π interactions. Several studies have been reported in which multipyridine-based tectons have been used to develop metallocycles and cages that can be tuned and controlled by design and chemical stimuli.^[3-13] These systems have been extensively investigated for drug delivery^[10-12] and catalysis. $\ensuremath{^{[13]}}$ Some examples of shape-persistent cyclic tectons bearing pyridine moieties have recently been reported and studied for their self-assembly or recognition properties^[14] based on their intrinsic porosity.^[15] Extrinsic porosity, in which the cavities are located between the molecules by the interplay of different intermolecular interactions, is another efficient method to obtain materials to be used for separation, catalysis or storage. By following this strategy, the Shimizu group has synthesised a pyridyl-bis-urea macrocycle assembling into a

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self-assembly properties, which influence their crystal structures and their ability to form co-crystals. Co-crystals of the tectons with tetraiododifluorobenzene were obtained both via traditional and mechanochemical crystallisation strategies, proving their potential use in crystal engineering. The energetic contributions of the supramolecular interactions at play in the crystal lattice have also been evaluated to better understand their nature and strength and to rationalise their role in designing molecular crystals.

columnar arrangement in the solid state. Despite the lack of pores, the material can take up guests such as trifluoroethanol, I₂, H₂ or CO₂.^[16,17] Furthermore, the columnar assemblies have been shown to adsorb and organise small guest molecules that interact via H-bonds.^[18] The same group reported the preparation of a wider bis-urea macrocycle, based on a pyridylacetylene scaffold, capable of acting as nanoreactor for the polymerisation of isoprene.^[19] Johnson and co-workers synthesised a library of inherently fluorescent pyridine-based urea receptors that were successfully employed in the sensing of Cl⁻ and other anions.^[20-25] The same group has recently reported a 3,5-bis((2-iodophenyl)ethynyl)pyridinium scaffold functionalised with a methanesulfonyl withdrawing group to polarise iodine halogen bonding units for anion binding.^[26] Similarly, Berryman and co-workers suggested a possible strategy to pre-organise pyridine-acetylene receptors via intramolecular hydrogen bond-halogen bonds (HB-XB).[27] The resulting planar receptor showed a ninefold increase in binding to halides (Iand Br⁻). Against this background, and with the aim of adding a group of versatile tectons to the toolkit of crystal engineers,^[28] we designed and synthesised four new V-shaped multidentate building blocks characterised by an aryl acetylene scaffold comprising three substituted pyridine rings connected by two triple bonds (Figure 1, left). The substituents on the two lateral pyridine rings-namely Br atoms (TBr), carboxylic groups (TA), triple bonds (TT) and amine groups (TN)-were chosen to endow the tectons with different steric, electrostatic (Figure 1, right) and self-assembly properties, so as to systematically study the differences in their resulting crystal structures. Moreover, in the solid state, the free rotation of the pyridine rings around the triple bonds allows the tectons to adopt three different conformations (C, S or W, respectively; Figure 1) depending on the relative orientation of the pyridyl rings.



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Figure 1. Left: Molecular sketch of the different conformations that the pyridine-based tectons (TBr, TA, TT and TN) can adopt by rotation around the acetylene bonds. Right: Molecular electrostatic potential surfaces for TBr, TA, TT and TN calculated at the B3LYP/6–311++G(d,p) level of theory using Gaussian 09 starting from the geometry present in their crystal structures.^[30] The colour code from red to blue indicate areas of rich (hydrogen/halogen-bond acceptor sites) and depleted (hydrogen-bond donor sites) electron density, respectively.

To test the behaviour of the tectons as halogen-bond acceptors, and to study how this would affect their self-assembly, we co-crystallised them with 1,4-diiodotetrafluorobenzene (DITFB), which has been widely used in crystal engineering for its ability to form N-I halogen bonds.^[29] The halogen bond is an interaction occurring between an electrophilic region (called σ -hole) associated with a halogen atom (the halogenbond donor) and a nucleophilic region (the halogen-bond acceptor).^[31] Thanks to its directionality, it has been widely used over the past 20 years in the field of supramolecular chemistry for designing molecular crystals.^[29c, 32] Halogen- and hydrogenbonding often compete in determining the outcome of supramolecular structures, giving rise to a plethora of different networks depending on the molecular geometries and the numbers and strength of the donors and acceptors involved.^[1e] Given the chemical nature of the tecton objects of the present study, the interplay between halogen- and hydrogen-bonding in directing the final solid-state structure was of particular interest. Single crystals suitable for X-ray diffraction were obtained for TBr, TN and TA, for which it was thus possible to analyse in detail the solid-state assembly. Crystals of TT were obtained only in combination with DITFB and will therefore be discussed in the relevant section.

Results and Discussion

Synthesis of the tectons

The tectons **TBr**, **TA**, **TT** and **TN** were obtained by following the retrosynthetic strategy shown in Scheme 1 (see the Supporting Information for a detailed discussion of the synthetic procedure). The disconnection of the triple bonds leads to pyridinic synthons. Functionalisation can be achieved by changing the substituents on the starting pyridine. The *tert*-butoxy group in the *para*-position on the central ring was selected to ensure solubility in most organic solvents.



Scheme 1. Retrosynthesis for TBr, TA, TT and TN. The first disconnection leads to synthons for Sonogashira coupling. The functional group for the coupling, halogen and triple bond, can be either on the axial or the central pyridine. Both options were tested. The combination giving the highest yield was used in the final syntheses.

Self-assembly of the tectons: The role of solvent and substituents

Scheme 2 highlights the sites of the V-shaped building blocks that can trigger the formation of supramolecular interactions (in particular hydrogen-bond, halogen-bond, or π - π stacking), along with a summary of the interactions at work in the crystal structures of **TBr**, **TN** and **TA**.

As bromine attached to a pyridine ring is a relative weak halogen bond donor, it is to be expected that hydrogen bonds and π - π stacking are the driving force in the crystal packing of the tectons.

Crystal structures of TBr

Crystals of **TBr** (which does not possess any strong H-bond donors) were grown by slow evaporation of different solvents, namely toluene, benzene, chloroform and methanol. The first three solvents were not included in the final structure, but they nevertheless influenced the polymorphic forms obtained, indicated as **TBrT**, **TBrB** and **TBrC**, respectively. Crystallisation from methanol led to a solvated form, **TBrM**.

In the molecular structure of **TBrT**, the tecton adopts a C conformation (Figure 1, Figure 2 A). The angles between the mean planes passing through the central ring (acetylene moieties included) and the two lateral pyridine fragments C8-C12/N2/Br1 and C15-C19/N3/Br2 are 55.85(6)° and 50.78(4)°, respec-

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Scheme 2. Top: Sites involved in the formation of supramolecular interactions in TBr, TN, TA. Bottom: summary of the main supramolecular interactions at play in the crystal structures of TBr, TN and TA (see discussion below).

tively. These lateral pyridine fragments are at an $87.99(6)^{\circ}$ angle with respect to each other. In the crystal structure, the **TBr** molecules pack through a series of C–H···N and π – π stacking interactions (Figure 2B). More precisely, each **TBr** acts both as donor and acceptor towards a symmetry-related molecule ii (ii = x–1, y, z), forming four distinct interactions [C11–H11···N2, 3.328(5) Å and 170.78(2)°; C12–H12···N1, 3.534(4) Å and 149.70(4)°; C18–H18···N3, 3.324(2) Å and 167.74(8)°; C19–H19···N1, 3.508(4) Å and 155.92(8)°]. On the other side, π – π stacking is present between the pyridine rings C15–C19/N3/Br2 and C8–C12/N2/Br1 (in position 1+x, 1/2-y, -1/2+z). The main geometrical parameters are the two distances centroid···C8 of 3.526(5) Å and centroid···C15 of 3.529(6) Å.

These sets of interactions contribute to the overall packing of the molecule, which is very compact without accessible voids (Figure 2 C). The synergistic effect of stacking and nonconventional H-bonding interactions seems to dominate over the formation of Br…N halogen bonding or Br…Br contacts of type I/II.^[33]



Figure 2. A) Molecular structure of **TBrT** with partial labelling Scheme. B) Relevant weak interactions in **TBrT**. Symmetry codes: i = 1 + x, 1/2 - y, -1/2 + z; ii = x-1, y, z. C) Packing in the crystal structure of **TBrT**. H atoms have been omitted for clarity.

As can be qualitatively seen in Figure 1, the depleted electron density areas (hydrogen-bond donor sites) in TBr are located around the H atoms of the aromatic rings and the tertbutyl groups. Indeed, analysis of the crystal structure of TBrT highlighted the tendency of the pyridyl moieties to act as Hbond acceptors towards the aromatic C-H groups (Figure 2B). Therefore, we decided to use benzene as crystallisation solvent, which could possibly template the crystal packing of TBr, being less sterically hindered than toluene. When crystals grown from benzene were analysed, no solvent appeared to be included, but a different polymorph of TBr was obtained (TBrB). In this case, the conformation of TBr turned out to be of the S type (Figure 1, Figure 3A) with the pyridine ring containing the nitrogen atom N3 pointing upwards with respect to N1 and N2. In TBrB, the molecules are more planar than in the previous case, as can be seen from the angles formed by the mean planes passing through the rings $[43.11(7)^{\circ}, 13.42(7)^{\circ}]$ and 33.16(8)°, following the description given for TBrT]. This different conformation is clearly connected with the overall

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Figure 3. A) Molecular structure of **TBrB** with partial labelling Scheme. B) Relevant weak interactions in **TBrB**. Symmetry codes: i=2-x, 1-y, 1-z; ii=1-x, 1-y, -z; iii=x-1, y, z. C) Packing in the crystal structure of **TBrB**. H atoms have been omitted for clarity.

crystal structure and the set of supramolecular interactions consolidating it (Figure 3 B).

In this case, each **TBr** molecule forms two sets of centrosymmetric C–H···N interactions with two other molecules in position i=2-x, 1-y, 1-z and ii=1-x, 1-y, -z, of the type C23–H23B···N3 [3.387(5) Å and 134.34(8)°] and C18–H18···N1 [3.492(4) Å and 157.58(7)°] with the *tert*-butyl C–H atoms as H-bond donors. A short π - π interaction is also present, involving the π cloud of one triple bond and the C15–C19/N3/Br2 ring of a **TBr** tecton in position iii=x–1, y, z [centroid···C13, 3.696(3) Å]. Finally, π - π interactions are present involving the pyridine rings N2/C8–C12 of adjacent molecules [not shown in

Figure 3 for clarity; the distance of the mean planes passing through the rings in position x, y, z and -x, 2-y, 1-z is 3.412(3) Å]. Also in this case, the final packing is extremely compact without any accessible permanent porosity (Figure 3 C).

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A third batch of crystals was grown from chloroform, yielding again the tecton in a C conformation (**TBrC**, Figure S36 A). The **TBrC** molecular structure is almost perfectly superimposable with that of **TBrT** grown from toluene. However, in the chloroform case, the molecule crystallises in the triclinic space group $P\bar{1}$ as opposed to the monoclinic P21/c of **TBrT**, leading to some minor differences in the crystal packing (Figure S36 B). In all three of the polymorphic forms (**TBrT**, **TBrB** and **TBrC**), the bromine atoms do not play an active role in the formation of supramolecular interactions. Their only influence on the packing is due to their steric hindrance.

In our crystallisation experiments, the only solvent that was included in the final structure was methanol, a "non-innocent" molecule capable of interacting via H-bonds, which yielded the solvated form **TBrM** with a 1:1 tecton/solvent ratio (Figure 4A). The conformation of the tecton is S, as in the case of **TBrB**.

The pyridine ring C8-C12/N2/Br1, which points upward with respect to the other two pyridine moieties, is held in place by a O1S-H10…N2 H-bond [2.975(3) Å, 171.23(6)°]. Besides this interaction, methanol plays no other role in the final crystal



Figure 4. A) Molecular structure of **TBrM**, highlighting the H-bond (blue dashed line) between one pyridine ring and the methanol molecule. B) Main weak interactions contributing to the overall general packing of **TBrM**: a) centroid···centroid interactions between pyridine rings. b) C–H···N and C–H···O interactions. c) C–H··· $\pi_{triplebond}$ interactions.

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packing, again featuring π - π and C-H…N interactions (Figure 4B). In particular, Figure 4Ba shows the weak π - π stacking involving the pyridine rings C8-C12/N1/Br1 and C15-C19/N2/ Br2 in position x, 1-y, 1/2+z [3.804(5) Å]. Furthermore, each TBr forms a supramolecular dimer held together by C-H-N interactions [C11–H11···N1(3/2-x, 3/2-y, 1-z), 3.434(2) Å and 144.03(2)°; C10-H10···N3(3/2-x, 3/2-y, 1-z), 3.506(4) Å and 152.66(7)°] (Figure 4Bb). Supramolecular dimers assemble in tetramers formed by two sets of weak centrosymmetric C-H---O hydrogen bonds [C21-H21B---O1(1-x, -y, 1-z), 3.619(4) Å and 158.01(4)°]. The tetramers assemble in a layer parallel to the (101) plane. In addition, a supramolecular dimer is also formed by the interaction of a C-H group from the pyridine molecule C15–C19/N2/Br2 and the electronic π cloud of the triple bond [C19-H19-C7(3/2-x, 1/2-y, 1-z), 3.646(4) Å and 145.82(8)°] (Figure 4 Bc).

Crystal structure of TN

Crystals of **TN** were obtained by slow evaporation of a chloroform solution. In this case, solvents capable of forming Hbonds were excluded, to avoid any influence on the packing of the ligand. **TN** is characterized by the presence of $-NH_2$ substituents on the lateral pyridine rings (characterised by a depletion of electron density, Figure 1) which are good H-donor moieties, and of the pyridyl fragments, which are good hydrogen-bond acceptors.

Hence, the main interaction directing the final crystal packing is H-bond with the formation of classic $R_2^2(8)$ [and also $R_2^2(18)$] synthons typical of aminopyridine groups (Figure 5 A). As shown in Figure 5 A, each of the $-NH_2$ groups and of the pyridine rings act as H-bond donor and acceptor, respectively, with two adjacent molecules, thus forming a chain along the *c*-axis direction [N3-H3NB···N1, 3.301(3) Å and 152.08(8)°; N3-H3NA···N2, 3.085(2) Å and 173.39(7)°; N5-H5NA···N1, 3.474(4) Å and 148.64(5)°; N5-H5NB···N4, 3.123(4) Å and 171.89(7)°]. The crystal structure is further consolidated by weak π - π stacking interactions involving the side pyridine rings [the centroid(blue)···centroid(red) distance is of 3.751(9) Å]. The overall crystal packing of **TN** consists of sets of H-bonded chains held together by van der Waals forces. As could be expected based on the functional groups present, the structure shows a very efficient occupancy of space with no accessible voids (Figure 5B).

Crystal structure of TA

The main feature of TA is the presence of two carboxylic groups, which are very effective H-bonding donor/acceptors moieties, with the C=O and the C-OH fragments displaying a negative and a positive region of electron density, respectively (Figure 1). Concomitantly, TA possesses very good H-bond acceptors: the nitrogen atoms of the pyridine rings. In theory, this tecton could assemble in supramolecular polymers through centrosymmetric dimeric O2-H2O-O3 and O4-H4O-O5 H-bonds or possibly create a macrocycle (Scheme S7), via the well-known R²₂(8) supramolecular homosynthon {---HOC==O}2. A dimeric species was indeed observed in the gas phase via ESI-MS spectrometry (Figure S15). However, crystals of TA were only obtained by slow evaporation of an acetone solution, which resulted in a monohydrate form [Figure 6A; O2–H2O···O1W, 2.600(2) Å and 173.88(4)°]. The dimeric Hbonded motif between the carboxylic acids of the pyridine



Figure 5. A) Molecular structure of **TN** showing the H-bonding motif connecting **TN** molecules along the *c*-axis direction. The molecules b and c are in positions 2-x, -y, -z and 2-x, -y, 1-z, respectively. The centroids of the pyridine rings are indicated as blue and red spheres. B) Packing of **TN** showing the reciprocal position of sets of H-bonded chains (highlighted in green, magenta, blue and orange), held together by van der Waals interactions.



Figure 6. A) Molecular structure of the monohydrate form of **TA**, highlighting the H-bond (blue dashed line) between the carboxylic acid of the pyridine ring and the water lattice molecule. B) View of the relevant interactions (shown as dotted lines) in the crystal structure of **TA**. One of the supramolecular chains is highlighted in blue. The chains form a layer parallel to (111) through H-bonds with the lattice water molecules.

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rings does not take place because of the lattice water molecule, but **TA** still forms H-bonded supramolecular chains C(18) (highlighted in blue in Figure 6B), based on the C=O···H-O synthon.

More precisely, the carboxylic oxygen atom O3 of one **TA** acts as hydrogen-bond acceptor towards the O4-H4O fragment of an adjacent molecule in position x, -1 + y, 1 + z, while the C=O5 moiety remains free [O4–H4A···O3, 2.694(2) Å and 164.36(4)°]. These chains are further bridged to form undulated layers parallel to the plane (111), with each water molecule acting as acceptor towards the O2-H2O group [O2–H2A···O1W, 2.600(2) Å and 173.88(4)°], and as donor towards the pyridine rings [O1W–H1W···N1(x, -1 + y, z), 2.968(3) Å and 149.70(6)°]. Finally, different layers are connected through van der Waals interactions, π – π stacking and H-bonding [O1W–H2W···N2(1–x, -y, 1–z), 2.926(5) Å and 165.57(4)°] to yield a compact structure without voids.

Co-crystallisation with DITFB

The systematic analysis of the crystal structures of the tectons showed their marked tendency to form tightly packed networks. As argued by Kitaigorodskii in his studies on organic crystals, molecules assemble to minimise free space.^[34] In our case, the assembly was driven by both hydrogen bonding and π - π stacking interactions, as expected. Furthermore, we observed a strong influence of the different functional groups on the pyridine rings and of the crystallisation solvents. Introducing **DITFB** to form a set of co-crystals was therefore a way to induce the formation of new networks exploiting the competition between halogen- and hydrogen-bonds with the pyridine rings.

As preliminary investigation, the crystallisation experiments were performed in a 2:1 tecton/DITFB molar ratio, to favour the assembly of the tecton around iodofluorobenzene. We carried out two types of crystallisation. The first type consisted of a "classic" method; namely, slow evaporation of a saturated solution. The second experiment comprised a liquid-assisted grinding (LAG) step, followed by re-crystallisation in chloroform, thus using the grinded powder as crystallisation seed^[35] (see the Supporting Information for experimental details). Several attempts of growing co-crystals of TA and DITFB both from solution and from grinding always yielded crystals of the two components alone, most likely because of the important role of H-bonding in directing the crystallisation of TA. In the case of TN, it was possible to obtain co-crystals with DITFB only by employing the LAG step, suggesting the potential of this technique.

Co-crystal TBr-DITFB

In the case of **TBr**, both methods yielded the same 1:1 co-crystal (Figure 7 A). In the asymmetric unit, the nitrogen atom N1 of the central pyridine ring is halogen bonded to the iodine atom 11 of **DITFB** [11...N1, 3.009(3) Å] (Figure 7 A). **TBr** adopts a W conformation (Figure 1), which is consolidated by a series of type II Br...Br interactions at 3.574(6) Å connecting the mole-



Figure 7. A) Molecular structure of the co-crystal formed by **TBr** and **DFTIB**. B) Packing of the co-crystal **TBr-DITFB**, showing two supramolecular chains formed by Br···Br interactions (orange dotted lines) propagating in two different directions. The chains are bridged by **DFTIB** molecules through halogen bonds (blue dotted lines). H atoms have been omitted for clarity. C) Centrosymmetric dimers formed by π - π stacking involving the aromatic rings of **TBr** and of **DITFB**. D) Crystal packing of **TBr-DITFB** viewed along the *b*-axis direction highlighting the voids as yellow cylinders.

cules in a chain. In the crystal, two sets of these chains are formed, oriented along different planes of the cell, that propagate at an angle of roughly 69° one with respect to the other. The chains are held together by **DITFB** molecules that bridge pairs of TBr tectons in a zig-zag fashion through halogen bonds 11...N1 [3.009(3) Å] and 12...N3(x, 3/2-y, 1/2+z) [3.058(3) Å] (Figure 7 B). One halogen bond involves the central pyridine, the second is formed with one of the two lateral pyridine rings (Figure 7 B), while the N atom of the third ring does not form any interaction.

In addition, centrosymmetric supramolecular dimers are formed by mutual π - π stacking of the lateral pyridine moieties [Cg1...Cg2ⁱ, 3.536(8) Å] and by the weak interaction of **DITFB** with the central ring of **TBr** [Cg3...Cg4ⁱ, 3.536(8) Å] (Figure 7C; symmetry code i = 1-x, 1-y, 1-z).

It is also possible to analyse the topology of the interactions present in the crystal structure of **TBr-DITFB** by means of the software ToposPro.^[36] In particular, the structure can be simplified to its standard representation by considering the centroids

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of the molecules **TBr** and **DITFB** as the nodes of the simplified net, connected through the halogen bonds N···I and Br···Br mentioned above. Successively, the final underlying net is obtained by deleting the 2-coordinated nodes represented by the bridging **DITFB** molecules, to yield a 4-c, **cds** net {6⁵.8} with vertex symbol [6.6.6.6.6(2).*]^[37] (see Figure S56 B). According to this analysis, in the structure there are four interpenetrating nets (see Figure S56 C) related both by translation and inversion, belonging to the Class IIIa.^[38]

Due to the interactions described above, the co-crystal assembles in a set of channels, parallel to the *b*-axis direction, which are filled with chloroform molecules (Figure 7D). The highly disordered solvent could not be sensibly modelled and was treated with the program SQUEEZE (see experimental section). In contrast to the tightly packed arrangements of the tecton alone, the overall structure shows ca. 23% of voids in the unit cell (as calculated by the program *PLATON* with a probe radius of 1.2 Å).^[39] This structure could potentially display an extrinsic porosity if its permeability without structural collapse/modification due to the removal of the solvent were to be demonstrated.^[40]

Co-crystal TN-DITFB

Tecton TN offered the possibility of analysing the effect (either orthogonal or competing) of concomitant strong hydrogen and halogen bonding interactions. The co-crystal between TN and **DITFB** was obtained only through grinding, since the crystals grown from slow evaporation of a solution of the two components turned out to be the two starting compounds. The asymmetric unit of TN-DITFB consists of a TN tecton in W conformation, two DFTIB molecules and adventitious water. The pyridine ring containing atoms N2 and N3 was found to be disordered over two positions, as was the water lattice molecule O1W. Figure 8A shows all the relevant supramolecular interactions that a molecule of **TN** in general position forms with symmetry-related water, TN and DITFB molecules through hydrogen (of medium to weak strength) and halogen bonds, respectively. [O1WA-N2A, 2.717(2) Å; O1WAⁱ-N3A, 2.930(2) Å; N5–H5N2···N5ⁱⁱⁱ and N5^{iv}–H5N2^{iv}···N5, 3.574(3) Å and 136.10(9)°; N1…I2B, 2.948(6) Å; N4…I2A, 2.966 Å; for symmetry codes see Figure 8A]. Different to what was observed in the crystal structure of TN, the amino moieties are involved in H-bonds either with each other or with water. Two of the pyridine rings act as halogen-bond acceptors, whilst the third interacts with water. One of the main features of the crystal packing is the presence of channels along the c-axis direction (Figure 8B). Such channels are centred around the sixfold axis of the hexagonal space group P64 in which the co-crystal crystallises. However, the channels are very small (3% of the unit cell volume calculated with a probe radius of 1.2 Å by the program PLATON)^[39] and they are occupied by some residual electron density found at 1.9-2.2 Å from O1W that can be ascribed to some further, unmodelled disorder of the water molecule.



Figure 8. A) View of the ligand **TN** forming supramolecular interactions with symmetry-related neighbouring molecules. Symmetry codes: i = x-y, x, 2/3+z; ii = -x+y, 1-y, 5/3+z; iii = -x+y, 1-x, -1/3+z; iv = 1-y, 1-x+y, 1/3+z. Only the H atoms of the amino groups are shown. B) Packing of **TN-DITFB** viewed along the *c*-axis direction. Water molecules and H atoms have been omitted for clarity. The channels are represented as yellow cylinders.

Co-crystal TT-DITFB

We then analysed the behaviour of the trimer TT, bearing triple bonds as substituents on the lateral pyridine rings (Figure 9A). In this case, the crystals were obtained directly from solution, but not from the grinding experiment. The asymmetric unit of the co-crystal comprises one TT molecule in a W conformation and two DITFB molecules. In the absence of substituents suitable for hydrogen bonding or adventitious water molecules, all the three pyridine rings are simultaneously involved in halogen bonds with **DITFB** molecules [I1Aⁱ...N1, 2.951(2) Å; I2A···N2, 2.942(2) Å; I2B···N3, 3.029(4) Å; for the symmetry code see Figure 9A]. The resulting 1:3 assembly is roughly planar, (Figure 9A); planarity is maintained in the crystal structure, which consists of layers parallel to the (-101)plane, consolidated by a series of weak C-H-F interactions involving both the C14-H14 acetylene moiety and the tert-butyl group [Figure 9B; F1B···H14–C14(1+x, y, 1+z), 2.62 Å, 3.181(3) Å and 118.30(7)°; C27–H27A-F4B, 2.66 Å, 3.576(4) Å and 155.67(8)°]. In this case, the packing does not show the presence of accessible voids, and no solvent is included. In the absence of bulky Br substituents or of moieties capable of forming strong H-bonds (such as the carboxylic acid or amino groups), the DITFB molecule can assemble around itself three

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Figure 9. A) View of the halogen bonds formed in the crystal structure of **TT-DITFB**. The molecule labelled *i* is in special position (i = x, 1 + y, z). B) Packing of **TT-DITFB** showing layers parallel to the (-101) plane and detail of the weak C–H…F interactions.

different **TT** tectons (one slightly off-set) by the synergistic effect of N···I and C–H···F interactions (Figure 10).

Scheme 3 summarises the most important features of the three co-crystals obtained. In general, the combination with **DITFB** shows a disruption of the compact crystalline packing



Figure 10. Stick (left) and space filling (right) assembly of TT molecules around a central DITFB.

observed in the structure of the tectons alone, paving the way for the possible formation of porous networks.

Interaction energy calculations

To better understand the supramolecular forces at play in the crystal structures described so far, we calculated the intermolecular interaction energies and visualised them through "energy frameworks"^[41] using the program CrystalExplore17.^[42] In this approach, which goes beyond the focus on specific atom-atom contacts, the total interaction energies (E_{tot}) are calculated starting from the crystal geometry using either a CE-B3LYP/6-31G(d,p) or a HF/3–21G level of theory. The total energy comprises four components; namely, the electrostatic (E_{ele}), polarisation (E_{pol}), dispersion (E_{dis}) and exchange-repulsion (E_{rep}) terms, which are also given as output of the calculation.

Once the energies have been determined, they can be graphically displayed in the form of frameworks, which are visualised as cylinders joining the centres of mass of the molecules in the crystal, with the cylinder radius proportional to the magnitude of the interaction energy in different directions.^[41b,d] Energy frameworks highlight the topology of the interaction energies between molecular pairs, and how particular contacts contribute to the crystal lattice energy. This approach can be extremely useful, for instance, when comparing polymorphs, thus providing a valuable tool to summarise gualitatively and quantitatively the strength of the interactions involved in the formation of the crystal structures. Details of the interaction energy frameworks obtained for the different tectons are reported in Section 4 of the Supporting Information. In summary, this investigation shows that, in the case of the TBr family, the most important contribution comes from dispersion interac-

		R = -Br	R = - NH ₂	R = -CCH
С(СН ₃) ₃	Halogen bonds	2	2	3
	N involved in halogen bonding	1,3	1,3	1,2,3
$H = \frac{1}{\pi} \frac{1}{\sqrt{\pi}} \frac{1}{\sqrt{\pi}} H$	Other interactions	Br···Br π-π stacking	N-H⋯N N-H⋯O	C-H…F
$\begin{array}{ccc} H & \uparrow & 2 \\ R & R \\ R & R \end{array}$	Packing features	Channels (~ 23% of void occupied by solvent)	Channels (~ 3% of void occupied by solvent)	Layers (no void)

Scheme 3. Schematic view of the main features in the crystal structures of DITFB with TBr, TN and TT.

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tions and particularly from π - π stacking, especially in the polymorph grown from benzene. For this reason, compact packings without accessible voids were observed with all the crystallisation solvents employed. Substitution of the bromine atom with the amino group or the carboxylic acid in **TN** and **TA** leads to an increase of the electrostatic contribution and a dominant role of hydrogen bonding. Especially in the case of **TA**, this leads to a higher complexity in the resulting tridimensional network.

In the case of the co-crystals with **DITFB**, which is itself an aromatic compound, π - π stacking is still a dominant interaction when **TBr** is employed. On the other hand, the energetic contribution of halogen bonding clearly increases in the co-crystals of **TT** and **TN**, the crystal structures of which are the result of a synergistic effect between the two types of interactions.

Conclusions

In this contribution, we have presented the synthesis and structural characterisation of four new multidentate pyridinebased building blocks as tectons for crystal engineering. These tectons possess a rigid, V-shaped aromatic scaffold comprising a pyridyl-acetylene system functionalised with different moieties that influence their solid-state assemblies. Their crystal structures are mainly driven by H-bonds, C–H $\cdot\cdot\pi$ and π – π interactions, with a preference towards the formation of tightly packed architectures (especially in the case of the bromine derivatives), that can be highly influenced by the presence of solvent in the lattice. The three pyridine rings in the V-shape arrangement make the tectons good halogen-bond acceptors, as shown by the co-crystallisation experiments with DITFB, and can be exploited to modify the crystal structures by forming potentially porous adducts, as in the case of TBr-DITFB. Identifying and evaluating the energetic contributions of supramolecular interactions to lattice energies is important to extract some design principles from similar and related crystal structures. Thus, we have calculated the intermolecular interaction energies and visualised them by means of the related energy frameworks. Due to the presence of three aromatic rings and two triple bonds, dispersion interactions are always to be reckoned with and favour the formation of layered structures. We think that these newly synthesised molecules can open several opportunities to obtain new materials endowed with specific properties, besides adding a piece to the puzzle of the empirically derived principles for the design of molecular crystals.

Experimental Section

Crystallographic data: Deposition numbers 2043712, 2043713, 2043714, 2043715, 2043716, 2043717, 2043718, 2043719, and 2043720 contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: crystal engineering \cdot ligand design \cdot noncovalent interactions \cdot self-assembly \cdot supramolecular chemistry

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