Accepted Manuscript

Synthesis and structural studies of new asymmetric pyridyl-tetrazole ligands for supramolecular chemistry

Ursula Sheridan, John F. Gallagher, John McGinley

PII: S0040-4020(16)31170-X

DOI: 10.1016/j.tet.2016.11.026

Reference: TET 28240

To appear in: *Tetrahedron*

Received Date: 11 August 2016

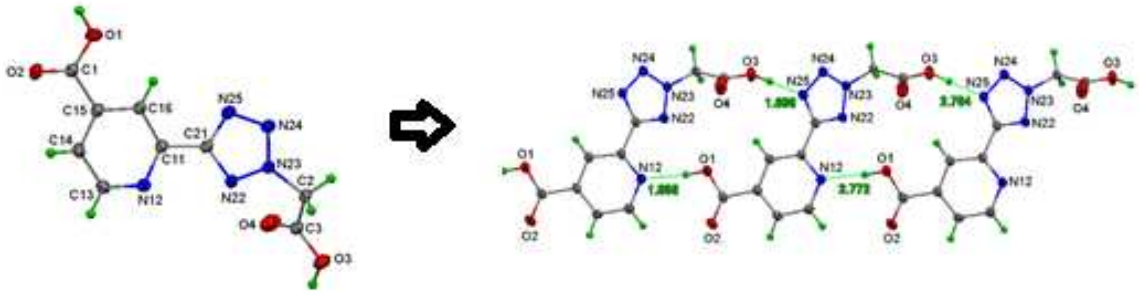
Revised Date: 26 October 2016

Accepted Date: 7 November 2016

Please cite this article as: Sheridan U, Gallagher JF, McGinley J, Synthesis and structural studies of new asymmetric pyridyl-tetrazole ligands for supramolecular chemistry, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.11.026.

Synthesis and structural studies of new asymmetric pyridyl-tetrazole ligands for supramolecular chemistry.

U. Sheridan, J. F. Gallagher, J. McGinley.



The synthesis of asymmetric diester derivatives of pyridyl-tetrazole ligands was successfully undertaken. Five crystal structures are reported including a dicarboxylic acid where the primary assembly, based on carboxylic…pyridine (COOH…N) synthons, forms an unusual cyclic hydrogen bonded ring with the $R^2_2(17)$ motif.

Synthesis and structural studies of new asymmetric pyridyl-tetrazole ligands for supramolecular chemistry.

Ursula Sheridan,[a] John F. Gallagher[b,*,†] and John McGinley.[a,*,#]

[a] Department of Chemistry, Maynooth University, Maynooth, Co. Kildare, Ireland,

[b] School of Chemical Sciences, Dublin City University, Dublin 9, Ireland.

Current address: Department of Chemistry, University of Copenhagen, DK-2100 Copenhagen Ø, Denmark.

† On sabbatical leave at CRM^2, Faculté des Sciences et Technologies, Université de Lorraine, BP 70239, Boulevard des Aiguelettes, 54506 Vandoeuvre-dès-Nancy, France.

* JMcG and JFG joint corresponding authors, email address john.mcginley@nuim.ie; john.gallagher@dcu.ie

Abstract

The synthesis of asymmetric diester derivatives of pyridyl-tetrazole ligands was successfully undertaken. Five crystal structures are reported including three asymmetric diesters (one of which is a mixed methyl ethyl ester derivative), a dicarboxylic acid and a monosodium (dicarboxylic acid)(monoacid-carboxylate) dihydrate intermediate. The dicarboxylic acid assembles by an unusual and unexpected route with the primary assembly based on carboxylic…pyridine (COOH…N) synthons that form an unusual cyclic hydrogen bonded ring with the $R^2_2(17)$ motif. Assembly in hydrogen bonding motifs using 'odd' numbers of atoms is the exception rather than the rule.

Keywords

Tetrazole, pyridine, synthesis, NMR, X-ray structures, asymmetric ligand.

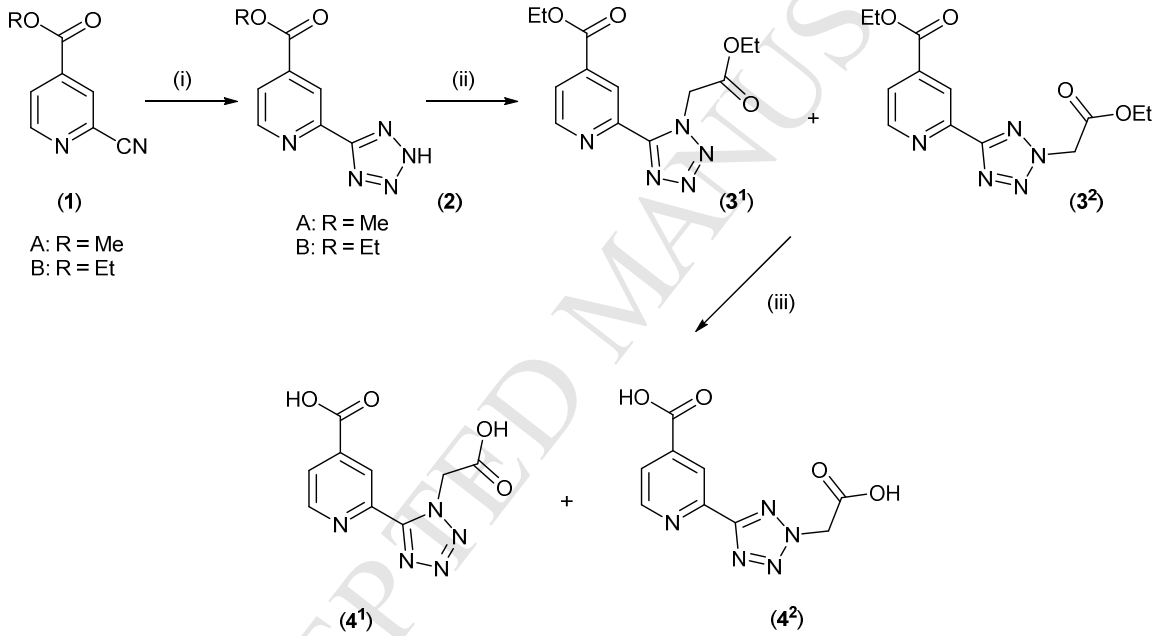
Introduction

Considerable attention has been paid to the design and synthesis of coordination polymer (CP) frameworks due to their applications in many areas e.g. gas storage, sensors, drug delivery.[1] The general synthetic strategy for designing such materials involves using multidentate ligands containing O- or N-donor groups, such as symmetric polycarboxylic acids and bipyridines. The majority of examples report the use of N-donor ligands as ancillary ligands, and these are often symmetrical ligands such as 4,4'-bipyridine.[2,3] N-Donor ligands can modify the structures and properties of the resulting materials by the cooperative coordination with carboxylate groups to meet the requirement of coordination geometries of metal ions in the assembly process.[2] In contrast, asymmetrical and flexible carboxylic acids have rarely been used, and the study on structures constructed from these type of ligands remains relatively under-developed, which may be attributed to the unpredictable structure types.[2] Wang and co-workers employed homophthalic acid, an asymmetrical carboxylate ligand, along with an N-donor auxiliary ligand, (1,4-bis(imidazol-1-yl-methyl)benzene), to construct CPs employing solvothermal methods.[4] The resulting networks exhibited diverse structures and coordination modes at the metal ions. Other authors have similarly utilised homophthalic acid in combination with other N-donor auxiliary ligands and have achieved interesting diverse structures.[5] Despite the success in employing this ligand as an asymmetric linker, there is a distinct paucity of examples utilising other asymmetric linkers. It is worth noting that much interest has been paid to tetrazole-based ligands as versatile building blocks, not only due to their variety of coordination modes but also because of their designable properties and potential applications.[6] Future developments and applications in chemistry will be devoted to exploiting asymmetry in catalysis, coordination polymers and materials science.

In our previous work, we successfully designed a series of pyridyl-tetrazole ligands with a tethered carboxylate group on the tetrazole ring and introduced them into CP systems, obtaining novel networks and multinuclear clusters.[6a,6b] The addition of another carboxylate on the pyridine ring would endow the linker with more coordinative possibilities and could be more conducive to forming higher dimensional infinite arrays. Furthermore, multifunctional linkers with both rigid and flexible carboxylic acid groups are severely under-investigated. Hence, we aimed to further develop the range of asymmetric carboxylate linkers while at the same time incorporating asymmetric N-donors into the linker (see Scheme 1). To the best of

our knowledge, there are no reports in the literature that employ a linker using both asymmetric nitrogen donors and mixed alkyl and aryl carboxylate groups. Accordingly, therefore, this report is the first to explicitly describe this approach.

Five crystal structures are reported herein; three of which are the asymmetric dicarboxylate esters **3[1]A**, **3[1]B** and **5**; a dicarboxylic acid **4[2]** and the monosodium sodium salt of a mixed dicarboxylic acid:monoacidcarboxylate ligand set **6**. The crystallographic methods used are as described in previous publications.[7,8,9] Diester structures **3[1]A**, **3[1]B** and **5** are described and compared given the importance of ester derivatives in a wide range of applications[10,11] together with the dicarboxylic acid **4[2]** and metallocarboxylate derivative **6**.



Scheme 1. Reaction conditions: i) NaN_3, LiCl, NH_4Cl, DMF, Δ, 8 h; ii) ethyl bromoacetate, K_2CO_3, MeCN, Δ, 24 h; iii) NaOH, MeOH/H_2O, Δ, 2 h.

Results and Discussion

The synthetic pathway chosen for the synthesis of the asymmetric carboxylate linkers is shown in Scheme 1. Synthesis commenced with a cyanation reaction which was undertaken utilising a modified method of that carried out by Huo and co-workers.[12] The initial reaction of the symmetrical pyridine N-oxide derivative was carried out in toluene, employing dimethylcarbamoyl chloride (DMCC) as the acylating agent and $Zn(CN)_2$ as the cyanide source. Analysis of the pale orange products, **1A** and **1B**, showed the three expected aromatic

resonances in the ^{1}H NMR spectra, as well as the presence of a nitrile group as a ν(C≡N) frequency positioned at 2237 cm^{-1} in the IR spectra. The obtained data for **1A** and **1B** were also consistent with literature reports,[13,14] indicating that our modified α-cyanation of a pyridine ring was successful. This method afforded comparable yields to those in literature reports (~65%) and offers a safer methodology as cheap $Zn(CN)_2$ is employed which is relatively less toxic than TMSCN, NaCN and KCN.

A 1,3-dipolar cycloaddition was then carried out using conditions utilised previously.[6a,6b,11,15] The presence of the tetrazole ring was alluded to as another aromatic ^{13}C signal was present in the ^{13}C NMR spectra of both **2A** and **2B**, accompanied by the concomitant disappearance of the nitrile ^{13}C peak. Consumption of the nitrile was also indicated by the disappearance of a ν(C≡N) frequency in the IR spectrum of **2A** and **2B**. Presence of a broad stretch positioned at 3083 cm^{-1} was attributed to a ν(N-H) frequency, which further pointed towards the presence of a protonated tetrazole ring. This broad stretch was not considered to be a carboxylic acid OH stretch as the presence of methoxy protons at 4.03 ppm and ethoxy protons at 1.38 and 4.43 ppm in the ¹H NMR spectra of **2A** and **2B**, indicated that the ester group remained intact. On recovery of the protonated 5-substituted tetrazole **2A**, issues were encountered in the acidic work-up. Yields were poorer than **2B**, and often following an extraction, the hydrolysed product was encountered. Although this result was not a considerable diversion from our intended synthetic route, there was concern over the feasibility of purifying regioisomers if a carboxylic acid was present. So it was decided to procede with the pyridyl ethyl ester derivatives only.

The alkylation of the tetrazole **2B** using ethyl bromoacetate in the presence of K_2CO_3 yielded two regioisomers, $\mathbf{3^1}$ and $\mathbf{3^2}$, where the superscript denotes the position of substitution of the functional group on the tetrazole ring. So, $\mathbf{3^1}$ indicates that the ester arm is attached at N-1 of the tetrazole ring and $\mathbf{3^2}$ indicates that the ester arm is attached at N-2 of the tetrazole ring. Analysis of the crude mixture of $\mathbf{3^1}$ and $\mathbf{3^2}$ by ^{1}H NMR spectroscopy revealed a ratio of ~10:12 of N-1 to N-2 isomers being produced, which represents a distinct lack of regioselectivity. The isomers were purified by flash column chromatography and identification and assignment of the position of the alkylated site was possible by analysis of the products by ^{13}C NMR spectroscopy.[16] The C-5 of the tetrazole ring resonated at ~152 ppm for the N-1 substituted isomer and ~165 ppm for the N-2 substituted isomer. The proton signals of the methylene group were more downfield for the N-1 isomers than for the N-2

isomers due to the anisotropic effects of the pyridine ring (Figure 1). The presence of the alkyl ester functionality was also confirmed by the presence of a second carbonyl ^{13}C peak at ~165 ppm in the ^{13}C spectra and also a second ν(C=O) frequency visible at ~1725 cm^{-1} in the IR spectra of the regioisomers.

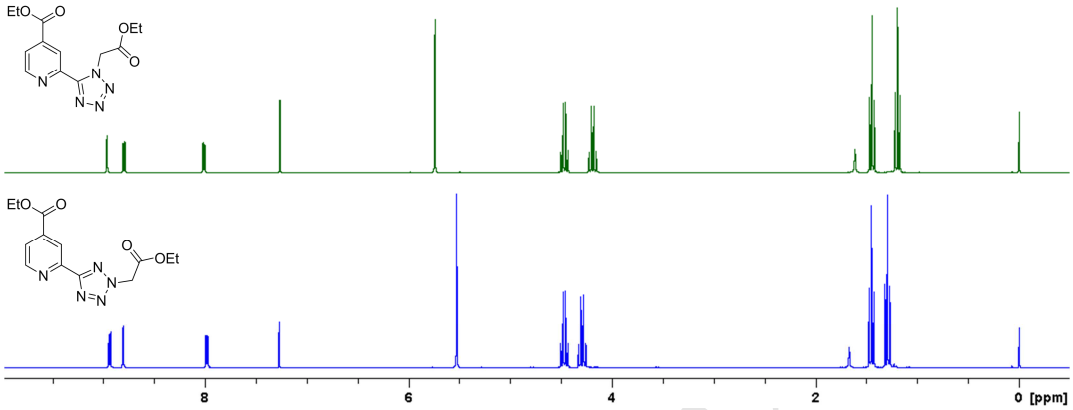


Figure 1. ^{1}H NMR spectra of **3**^{1} (green) and **3**^{2} (blue) obtained in $CDCl_3$.

Single crystals of **3**^{1}**A** (a dimethyl ester) and **3**^{1}**B** (a diethyl ester) together with a mixed diester (methyl/ethyl ester) product, **5**, were analysed by single crystal X-ray diffraction methods and confirmed the structures of the three compounds and established the geometries (see Figures 2, 3 and 4). Compound **5** resulted from a trans-esterification reaction that occurred in the methanol solution which originally contained the compound **3**^{1}**A**. As such, diesters are common organic compounds[11,17,18] and usually synthesised enroute to the mono- or dicarboxylic acids.[17] Table S1 contains pertinent crystallographic data for the **3**^{1}**A**, **3**^{1}**B** and **5** diester crystal structures and the structure of the dimethyl ester **3**^{1}**A** is shown in Figure 2. This reveals that the 5-membered tetrazole ring is essentially coplanar with the 6-membered pyridine ring at an angle of 0.5(2)° (Table 1) and the 4 atom aromatic carboxylate group is almost coplanar with the pyridine ligand 0.8(3)°. However, in contrast with this the 5 atom aliphatic carboxylate group is almost orthogonal with the tetrazole ligand at 81.36(17)°. In the crystal structure there are no classical hydrogen bonding interactions and for all three diesters there are no strong hydrogen bonding donors present as noted in our previous diester structures.[11] In **3**^{1}**A** the hydrogen bonding comprises an intramolecular C-H…O and C-H…N interaction per molecule as well as weak intermolecular C-H…N/O and π…π stacking interactions.[19] Some notable contacts include O1…C4 (linking aromatic and aliphatic esters of neighbouring molecules) and C2….N24 (tetrazole nitrogen of a neighbouring molecule) at 3.195(8) Å. In addition the cyclic $R^2_2(8)$ arrangement about inversion centres involving C3-

H3A…N23, together with two weak intermolecular hydrogen bonds involving C5-H5A…O2 and C13-H13…O3 complete the interactions and contacts.

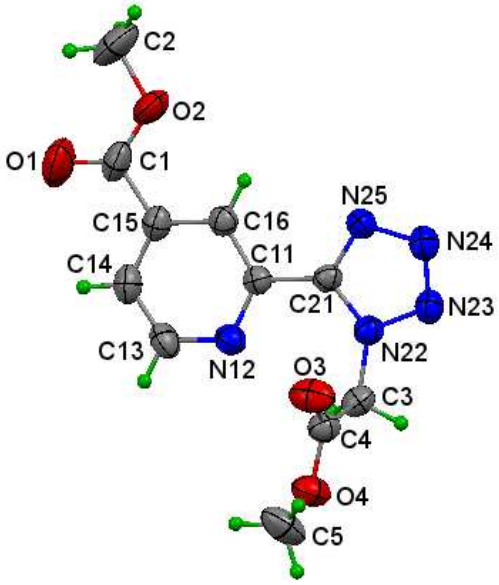


Figure 2. An ORTEP diagram of **3[1]A** with displacement ellipsoids at the 30% level.

Table 1. Interplanar angles (°) in compounds **3[1]A**, **3[1]B**, **4[2]**, **5** and **6**.

	3[1]A	**3[1]B** (molecules A, B)	**4[2]**	**5**	**6**
C_5N/CN_4	0.5(2)	3.30(16); 11.32(16)	16.22(6)	10.87(9)	10.32(5); 8.9(4)
Ester/C_5N	0.8(3)	6.8(2); 16.6(2)	2.95(13)	4.32(15)*	15.00(10);17.05(10)
Ester/CN_4	81.36(17)	74.30(13); 68.49(14)	77.95(7)	79.56(7)*	83.41(6); 82.94(6)

*=carboxylic acid group

The structure of the diethyl ester **3[1]B** is depicted in Figure 3a and displays the two crystallographically independent molecules (A) and (B) in the asymmetric unit. These molecules differ significantly (Table 1) as evidenced from the intramolecular distances spanning the molecules as O1…O3 = 8.522(3) Å and 8.360(3) Å for (A) and (B), respectively, (for $C3_{A/B}$…$C7_{A/B}$, this distance is 10.970(7) Å and 10.787(7) Å). The solid-state structure of **3[1]B** exhibits coplanarity between the tetrazole and pyridine rings for molecule A forming a dihedral angle of 3.30(16)°, while there is slight twisting between these two rings in molecule B, with a dihedral angle of 11.32(16)°. The pyridyl ester group is rotated slightly out of plane with the pyridine ring at 6.8(2)° and 16.6(2)° for molecules A and B, respectively. In contrast the tetrazolyl ester group is almost orthogonal with the tetrazole ligand at 74.30(13)° and 68.49(14)° for A and B, respectively. As for **3[1]A** above, molecules of **3[1]B** are essentially flat apart from the aliphatic ester group which is oriented

almost orthogonal to the rest of the molecule for both (A) and (B) molecules. As for **3[1]A** above, there are no classical interactions and the interactions are intramolecular and comprise four C-H…O/N intermolecular per asymmetric unit pair (A, B). Molecule A is involved in more intermolecular interactions and contacts than molecule B and typically with symmetry related molecules of A with molecules aggregating in double layers (Figure 3b). Of further interest is that the three diesters **3[1]A**, **3[1]B** and **5** have packing indices of 67.0, 67.6 and 67.8, respectively, and lower than the 71.0 and 72.9 for **4[2]** and **6** that contain stronger hydrogen bonding and charged entities, respectively.[9] The structural data for the former three **3[1]A**, **3[1]B** and **5** diester structures highlights the poorer overall packing and the lack of strong intermolecular interactions in their respective structures.[11] In fact, ester groups in crystal structures often exhibit large displacements about mean atom positions due to poor packing. In a previous paper, two related diesters exhibited a lack of strong interactions with packing indices of 67.2 and 67.3.[9,11] Often disorder is quite a common occurrence especially in the longer chain esters incorporating ethyl, n-propyl, t-butyl groups as in calix(n)arenes.[10,20]

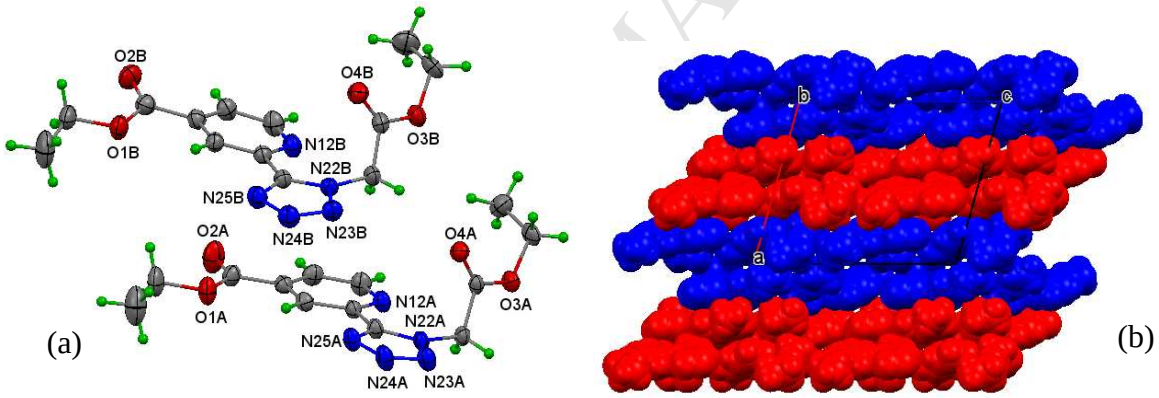


Figure 3. (a) An ORTEP diagram of the two independent molecules in the asymmetric unit of **3[1]B** with displacement ellipsoids at the 30% level (left): O and N atoms are labelled for clarity; Molecule A is labelled with A's while molecule B is labelled with B's. (b) A packing diagram of the sheets of (A) red and (B) blue highlighting the double layers of both molecules (right).

The molecular structure of the mixed diester **5** is depicted in Figure 4a. The transformation of an ethyl ester to a methyl ester in an organic molecule is a common occurance.[21] The normal reaction conditions for this transesterification process to occur require an alcohol (methanol in this case), the ester and also a catalytic amount of acid. In this case, we tried to react the ethyl ester ligand in methanol with zinc chloride and sodium hydroxide and got

transesterification instead of metal ion complexation. So, the zinc salt is acting as the proton source in this case. However, mixed esters are not uncommon and a review of the Cambridge Structural Database reveals many examples.[18] The solid-state structure of **5** shows a slight twist of 10.87(9)° between both tetrazole and the pyridine rings. The pyridyl carboxylate ester group is slightly out of plane with the pyridine ring at 14.32(15)° while the tetrazolyl carboxylate is close to being orthogonal with the tetrazole ligand 79.56(7)°. Although there are no classical hydrogen bonds present, the crystal structure benefits from having three distinct C-H…O/N interactions involving C4 (x2 interactions) and C6 with distances (D…A) from 3.327(3) to 3.446(4) Å and angles (D-H…A) from 159° to 171°. There are also a couple of short π…π contacts of note as depicted in (Figure 4B) with an interaction between the aromatic pyridine (C13, C14) and pyridine-tetrazole bridge atoms (C11, C21) of alternate molecules of 3.306(3), 3.334(3) and 3.353(2) Å.

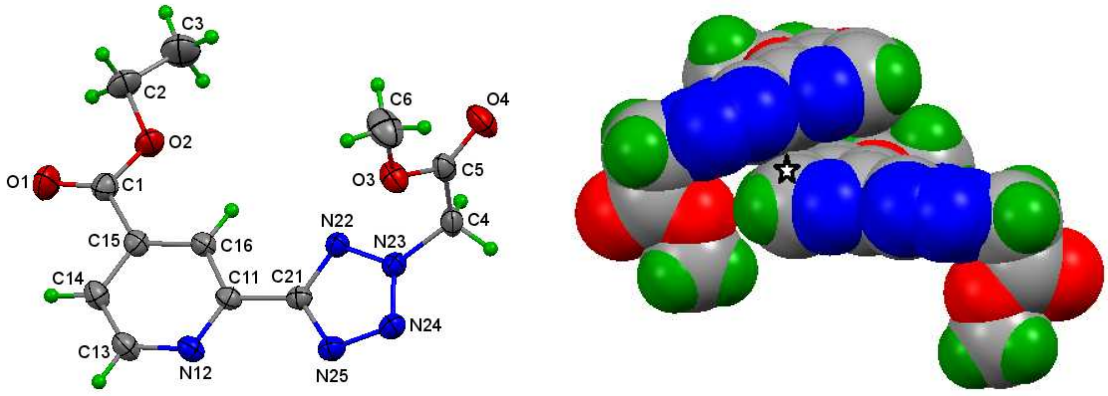


Figure 4. An ORTEP diagram of **5** with atoms drawn at the 30% displacement ellipsoids. A view of the short π..π contact of 3.3 Å (marked ★) with atoms depicted as their van der Waals spheres.

The reactions of the compounds $\mathbf{3^1}$ and $\mathbf{3^2}$ with NaOH were carried out in a mixture of methanol and water to give, on work-up with dilute acid, their respective dicarboxylates, $\mathbf{4^1}$ and $\mathbf{4^2}$, as previously reported.[6a] The ^{1}H NMR spectra of compounds $\mathbf{4^1}$ and $\mathbf{4^2}$ showed a complete absence of proton signals associated with ethyl groups. Furthermore, the IR spectra of both compounds showed the presence of the characteristic band for the protonated carboxylate group (~1724 cm^{-1}),[22] indicating the complete hydrolysis of the ester groups had occurred.

Dicarboxylic acid ligands are attractive as bidentate ligands for coordination chemistry.[11,23] As such, **4²** offers several roles as a potential multi-purpose ligand in coordination chemistry especially as it also contains aromatic N donor atoms for further use in potentially binding metal ions.[11] Single crystals of a dicarboxylic acid **4²**, as well as those of a second hydrolysis product **6**, were analysed by single crystal X-ray diffraction. Table S1 contains the pertinent crystallographic data for both crystal structures **4²** and **6**. The molecular structure of **4²** is shown in Figure 5 and reveals that the 5-membered tetrazole ring is twisted with respect to the 6-membered pyridine ring at an angle of 16.22(6)° with the 3 atom carboxylic acid group being almost coplanar with the pyridine ligand (2.95(13)°) whereas the 4 atom carboxylic acid group is almost orthogonal with the tetrazole ligand at 77.95(7)°.

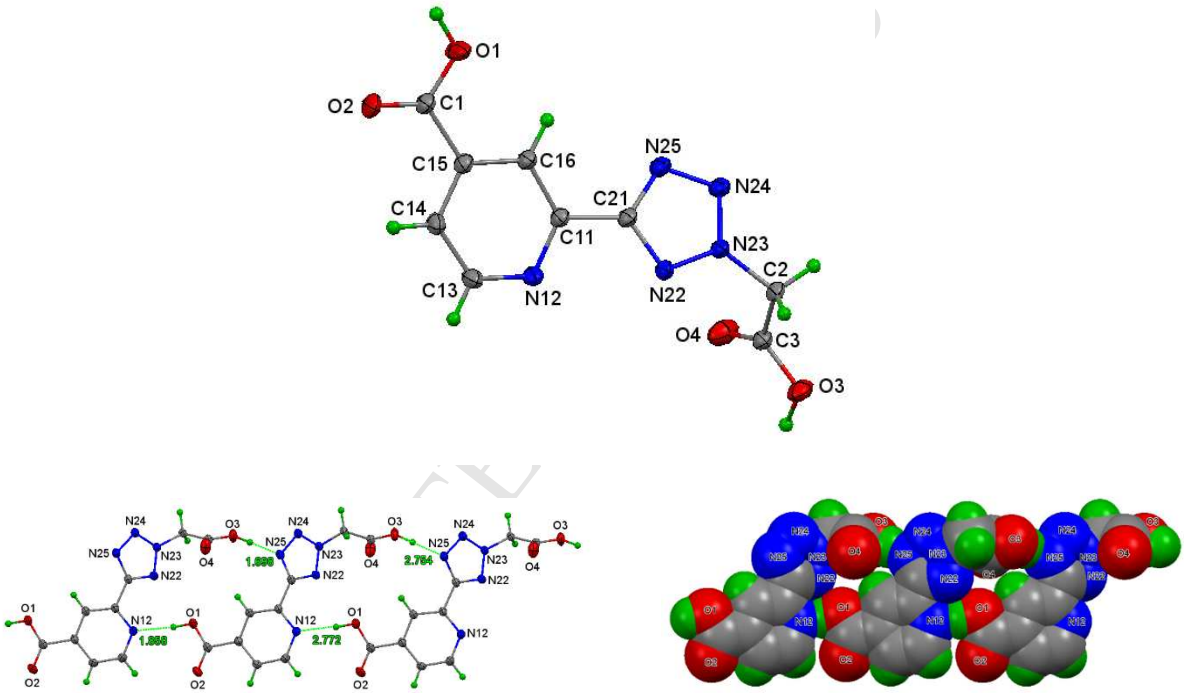


Figure 5. (a) An ORTEP diagram of **4²** with displacement ellipsoids at the 30% level; (b) An ORTEP of **4²** showing the aggregation along the *c*-axis direction with displacement ellipsoids at the 30% level with H…N and O…N distances (Å) and an CPK plot of **4²** showing the aggregation along the *c*-axis direction highlighting the O-H…N hydrogen bonding with atoms as their van der Waals spheres.

Molecules of **4²** do not aggregate by typical carboxylic acid dimer formation as would be expected by (*a*) a combination of identical carboxylic acid units forming dimers or (*b*) mixed carboxylic acid aggregation using the common $R^2_2(8)$ aggregation motif, or even (*c*) the

asymmetric association of an acid and a group such as (C2, N23, N24).[20,23] It is presumed that crystallisation does not occur by these expected (and other) though complex crystallisation pathways using *known synthon* assembly routes. Instead (and due to competition from the available N acceptor atoms) asymmetric aggregation arises with both of the carboxylic O-H groups (O1-H1, O3-H3) forming two O-H…N interactions with the N atom acceptors $N12_{pyridine}$ and $N25_{tetrazole}$ resulting in an asymmetric hydrogen bonded ring with motif $R^2_2(17)$. Of interest the aromatic carboxylic acid donor O1-H1 forms an interaction with the pyridine N12 atom at 2.7716(17) Å and the aliphatic carboxylic acid group O3-H3 with the tetrazolyl N25 atom with O3…N25 = 2.7542(17) Å. Interestingly, the O1-H1 group forms a close but repulsive contact with N22 (2.9017(17) Å) in the aggregation process with H1…N22 = 2.56(3) Å. (Figure 5b). There is no additional supporting C-H…O interaction for either of the O-H…N interactions with H…N = 2.89 and 2.78 Å. This contrasts with the common carboxylic acid supramolecular synthon (as $R^2_2(7)$) in carboxylic acid:pyridine structures where weaker C-H…O interactions augment the strong O-H…N interaction.[19,24]

The overall effect of the reciprocal carboxylic acid…N atom interactions as the $R^2_2(17)$ motif is to form 1-D chains along the *c*-axis direction (Figure 5c). Chains are linked into sheets and parallel with the (010) plane, that are further linked into a 3-D structure by two moderate C-H…O=C intermolecular interactions per molecule and additional weaker C-H…O=C interactions. Of further interest is that there is also a short intermolecular tetrazole N22…C1 contact of 3.168(2) Å between symmetry related molecules. The crystal structure of $\mathbf{4^2}$ represents an unusual structure containing unexpected assembly and highlights once again the unpredictable nature of self-assembly and especially in structures containing a range of potential donors and acceptors.[20b]

When further crystals from the solution containing the compound $\mathbf{4^1}$ were obtained, the structure of **6**, (which can be regarded as an intermediate between the diester and diacid) as shown in Figure 6, was obtained. The asymmetric unit in **6** comprises a sodium ion (Na^+), two water molecules, a dicarboxylic acid (A) and a monocarboxylic acid (B), that is deprotonated at the pyridyl carboxylic acid moiety. These revealed the local coordination of the sodium ions is by two water molecules, three carboxylic acid moieties and a carboxylate group of the two ligands. The carboxylic acid and carboxylate bond lengths clearly show whether the acid functionality is present or deprotonated as the carboxylate ligand, for all

four moieties. Overall, the charge is balanced by the Na^+ ion and the carboxylate ligand in (B). The resulting structure aggregates from octahedral sodium ion coordination and strong hydrogen bonding.

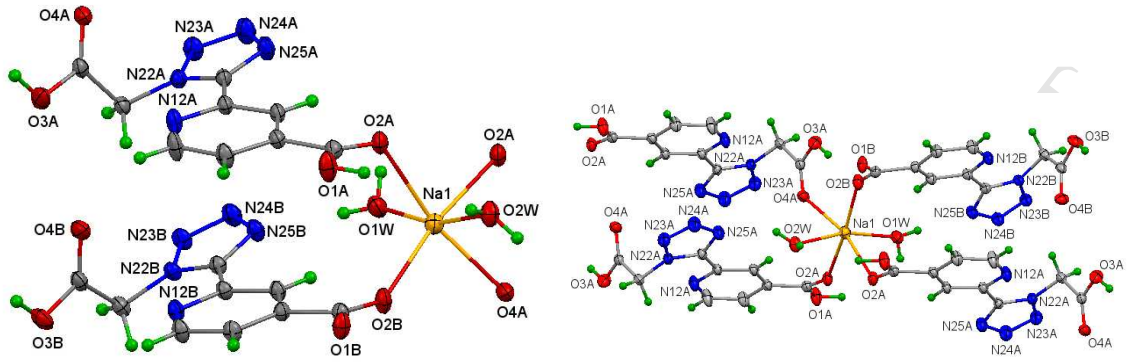


Figure 6. An ORTEP of **6** with atoms drawn at the 30% displacement ellipsoids and highlighting the similarity between the protonated dicarboxylic acid ligand A and deprotonated acid carboxylate ligand B and the quasi octahedral shell of O ligands about Na1 cation. A reverse view showing the complete ligand set involved in the sodium ion coordination.

Each sodium ion is coordinated by two water molecules O1W and O2W that are approximately *trans* to one another at 165.09(6)° with Na-O bond lengths of 2.3978(16) and 2.3821(15) Å. Three of the remaining sites are occupied by two O2A (O=C) atoms with Na-O of 2.4870(14) and 2.6286(15) Å and O4A (O=C) atom of three symmetry related dicarboxylic acid molecules (A) at 2.3254(13) Å and the sixth site by O2B of the carboxylate group in molecule (B) (2.3778(15) Å). The complexation is additionally strengthened by all O-H atoms participating in strong hydrogen bonding with the two water molecules and three carboxylic acid O-H's combining to give a network of strong interactions (Figure 7). The monocarboxylic acid ligand (B) is a receptor for five of these strong interactions and molecule (A) for only one. These seven O…N/O hydrogen bonding distances range from 2.539(2) to 2.970(2) Å and with O-H…N/O angle ranging from 146(2)° to 178(4)°.

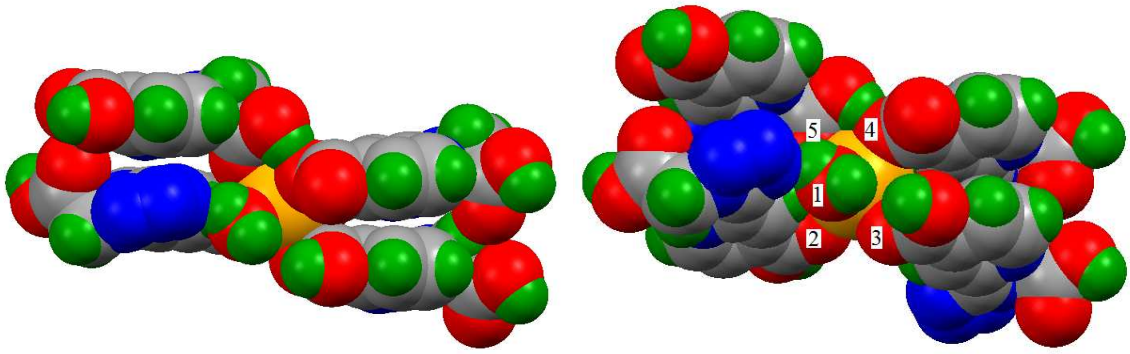


Figure 7. A CPK view of a section of **6** showing the octahedral binding about the Na^+ ion, the 6th coordination site is filled by a second water molecule *trans* to the water at position 1.

A close examination of the three carboxylic acids and carboxylate group shows an exquisite range of the type of interactions present. The carboxylic acid group for molecule (A) forms an 8-membered cyclic ring comprising (O1A, O2A), Na^+, O2W and O1B whereas (O3A, O4A) forms a tighter connected 6-membered ring as (O3A, O4A), Na^+ and O2B. For molecule (B), the O1B and O2B participate with the molecule (A) carboxylic acids and water molecule O2W hydrogen bonding whereas (O3B, O4B) forms the common cyclic 8-membered dicarboxylic acid hydrogen bonded dimeric units with graph set $R^2_2(8)$.[20] Of further note is that O1W links with a symmetry related O2W and this with the bridging O2A carboxylic acid O=C moiety gives rise to the dimeric unit of sodium ions connected by O2A and the two water molecules. As well as this both water molecules form O-H…N interactions with N25 of the tetrazole groups in molecules (A) and (B). The overall packing diagram is quite complex but the strong hydrogen bonding and interactions are clearly maximised with excellent packing efficiency.[9]

Conclusions

This paper deals with the further development of asymmetric organic pyridyl-tetrazole linkers, as previously reported,[6a,6b,16] by the introduction of a second carboxylate group onto the pyridine ring, in order to enhance the ability of the pyridyl tetrazole unit to form novel diverse high dimensional frameworks. Hence, the carboxylic acid derivatives **4**^{1} and **4**^{2} were synthesised from **3**^{1} and **3**^{2}, the ester derivatives, whose synthesis started from isonicotinic acid. Five crystal structures are reported including three asymmetric diesters (one of which is a mixed methyl ethyl ester derivative), a dicarboxylic acid and a monosodium (dicarboxylic acid)(monoacid-carboxylate) dihydrate intermediate. The dicarboxylic acid **4**^{2} assembles by

an unusual and unexpected route with the primary assembly based on carboxylic…pyridine (COOH…N) synthons that form an unusual cyclic hydrogen bonded ring with the $R^2_2(17)$ motif. Assembly in hydrogen bonding motifs using odd numbers of atoms is the exception rather than the rule. In complex **6**, both carboxylic acid groups are involved in the coordination of the sodium ions, with the pyridyl-tetrazole linker acting as a bridging group between pairs of sodium ions.

In contrast to the prolific bipyridine dicarboxylate ligands used in CP synthesis,[25] studies on asymmetric ligands, like $\mathbf{4}^{\mathbf{1}}$ and $\mathbf{4}^{\mathbf{2}}$, are much less developed. However, as demonstrated here, the potential to obtain interesting and diverse structures with such asymmetric structures is great and indicate that studies on these and related asymmetric ligands should be investigated further.

Experimental

Materials and methods

^{1}H and ^{13}C NMR (δ ppm; J Hz) spectra were recorded on a Bruker Avance 300 MHz NMR spectrometer using saturated $CDCl_3$ or d_6-DMSO solutions with a $SiMe_4$ reference, with resolutions of 0.18 Hz and 0.01 ppm, respectively. Infrared spectra (cm^{-1}) were recorded as KBr discs or liquid films between NaCl plates using a Perkin Elmer System 2000 FT-IR spectrometer. Solution UV-Vis spectra were recorded using HPLC grade solvents using a Unicam UV 540 spectrometer. Melting point analyses were carried out using a Stewart Scientific SMP 1 melting point apparatus and are uncorrected. Electrospray (ESI) mass spectra were collected on an Agilent Technologies 6410 Time of Flight LC/MS. Compounds were dissolved in acetonitrile:water (1:1) solutions containing 0.1% formic acid, unless otherwise stated. The interpretation of mass spectra was made with the help of the program "Agilent Masshunter Workstation Software". Starting materials were commercially obtained and used without further purification. Solvents used were of HPLC grade. Compounds **1A**[13] and **1B**[14] have been previously reported.

Caution! *Nitrogen-rich compounds such as tetrazole derivatives are used as components for explosive mixtures.*[26] *In our laboratory, the reactions described were run on a few gram scale, and no problems were encountered. However, great caution should be exercised when heating or handling compounds of this type.*

Synthesis of methyl-2-cyanoisonicotinate (**1A**)

A reaction mixture of 4-(methoxycarbonyl)pyridine-1-oxide[27] (0.20 g, 1.30 mmol), dimethylcarbamoyl chloride (DMCC, 0.12 mL, 1.30 mmol) and $Zn(CN)_2$ (0.23 g, 1.96 mmol) in toluene (15 mL) was heated to reflux under an argon atmosphere for 6 h. The reaction mixture was cooled to room temperature and deionised H_2O (10 mL) was added, and stirring was continued for 15 min. The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure to yield an orange solid (0.21 g, 65%) which required no further purification. m.p. 100-103 °C; ν_{max}(KBr) 2958, 2852, 2237, 1726, 1441, 1397, 1298, 1209, 1116, 974, 934, 882, 869, 765 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.90 (1 H, dd, *J* 4.9, 0.8 Hz, pyr-H), 8.24 (1 H, dd, *J* 1.5, 0.8 Hz, pyr-H), 8.07 (1 H, dd, *J* 4.9, 1.5 Hz, pyr-H), 4.01 (3 H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 162.6 (C=O), 151.0, 137.7, 133.8, 126.6, 125.0, 115.5 (CN), 52.3 (OCH_3); HRMS (ESI): $[M+H]^+$, found 163.0509. $C_8H_7N_2O_2$ requires 163.0502. NMR data is in agreement with literature data.[13]

Synthesis of ethyl-2-cyanoisonicotinate (**1B**)

A reaction mixture of 4-(ethoxycarbonyl)pyridine-1-oxide[28] (3.64 g, 21.82 mmol), DMCC (3.01 mL, 32.73 mmol) and $Zn(CN)_2$ (3.84 g, 32.73 mmol) in toluene (40 mL) was heated under reflux under an argon atmosphere for 2 h. The reaction mixture was cooled to room temperature and H_2O (30 mL) was added, and stirring was continued for 15 min. The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure to yield a brown solid. This was then passed through a silica plug using EtOAc:Pet. Ether in a 2:1 ratio as the eluent yielding a yellow oil which solidified on ice. Orange solid (3.28 g, 85%). m.p. 39-40 °C (lit. 42-44 °C);[14] ν_{max}(KBr) 2988, 2964, 2238, 1728, 1597, 1557, 1470, 1402, 1393, 1370, 1298, 1281, 1202, 1113, 1015, 990, 918, 890, 862, 763, 686 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.90 (1 H, dd, *J* 4.9, 0.9 Hz, pyr-H), 8.25 (1 H, dd, *J* 1.5, 0.9 Hz, pyr-H), 8.10 (1 H, dd, *J* 4.9, 1.5 Hz, pyr-H), 4.47 (2 H, q, *J* 7.1 Hz, OCH_2), 1.44 (3 H, t, *J* 7.1 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 163.1 (C=O), 151.9, 139.0, 134.7, 127.6, 126.1, 116.6 (CN), 62.6 (OCH_2), 14.1 (CH_3); HRMS (ESI): $[M+H]^+$, found 177.0659. $C_9H_9N_2O_2$ requires 177.0659. NMR data is in agreement with literature data.[14]

Synthesis of methyl-2(1H-tetrazol-5-yl)isonicotinate (**2A**)

Compound **1A** (0.20 g, 1.25 mmol), NaN_3 (0.09 g, 1.38 mmol), NH_4Cl (0.07 g, 1.38 mmol) and LiCl (0.03 g, 0.62 mmol) were heated at 110 °C in DMF for 12 h. The reaction mixture was filtered and the filtrate concentrated under reduced pressure. The residue was then taken up in deionised H_2O and 1 M HCl was added slowly until precipitation initiated. The mixture was then filtered and the solid dried. Brown solid (0.15 g, 62%). m.p. 163-166 °C; ν_{max}(KBr) 3071, 2922, 1724, 1547, 1438, 1416, 1393, 1336, 1295, 1270, 1247, 1198, 1173, 1054, 1031, 967, 755, 746 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.01 (1 H, d, *J* 4.9 Hz, pyr-H), 8.56 (1 H, s, pyr-H), 8.04 (1 H, d, *J* 4.9 Hz, pyr-H), 4.03 (3 H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 164.3 (C=O), 153.3, 151.4, 144.9, 138.6, 124.5, 121.0, 53.0 (OCH_3); HRMS (ESI): $[M+H]^+$, found 206.0677. $C_8H_8N_5O_2$ requires 206.0673.

Synthesis of ethyl-2(1H-tetrazol-5-yl)isonicotinate (**2B**)

Compound **1B** (2.28 g, 12.93 mmol), NaN_3 (0.93 g, 14.22 mmol), NH_4Cl (0.76 g, 14.22 mmol) and LiCl (0.27 g, 6.47 mmol) were heated at 110 °C in DMF (20 mL) for 12 h. The reaction mixture was cooled to room temperature, filtered and the filtrate was concentrated under reduced pressure. The remaining residue was redissolved in deionised H_2O and 1 M HCl was added dropwise until precipitation was initiated. When the formation of a precipitate ceased, the mixture was filtered. The collected precipitate was recrystallised from hot EtOH, yielding white crystals which were filtered off and washed with cold EtOH. White crystalline solid (2.13 g, 75%). m.p. 186-191 °C; ν_{max}(KBr) 3085, 2900, 2751, 1721, 1613, 1566, 1468, 1445, 1421, 1384, 1367, 1317, 1289, 1248, 1216, 1140, 1120, 1025, 1000, 896, 865, 762, 745, 726, 683 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.01 (1 H, d, *J* 4.9 Hz, pyr-H), 8.56 (1 H, s, pyr-H), 8.04 (1 H, d, *J* 4.9 Hz, pyr-H), 4.43 (2 H, q, *J* 7.2 Hz, OCH_2), 1.38 (3 H, t, *J* 7.2 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 163.7 (C=O), 154.5, 151.4, 144.8, 138.8, 124.6, 121.0, 62.0 (OCH_2), 13.9 (CH_3); HRMS (ESI): $[M+H]^+$, found 220.0830. $C_9H_{10}N_5O_2$ requires 220.0829.

Synthesis of ***3^1*** *and* ***3^2***

The tetrazole derivative (**2B**, 5.93 mmol) was heated to reflux with K_2CO_3 (0.90 g, 6.52 mmol) in MeCN (20 mL) for 30 min. Ethyl bromoacetate (1.09 g, 6.52 mmol) was added to the mixture and the reaction was further heated to reflux for 24 h. The reaction was then

cooled to room temperature and filtered and the filtrate was concentrated under reduced pressure. The remaining residue which consisted of two isomers was separated by column chromatography using Pet. Ether:EtOAc (2:1) as the eluent. The two regioisomers were recrystallised from a mixture of DCM and Pet. Ether.

Ethyl 2-(1-(2-ethoxy-2-oxoethyl)-1H-tetrazol-5-yl)isonicotinate (**3^1**)

White solid (0.65 g, 37%). m.p. 78-80 °C; ν_{max}(KBr) 2980, 2908, 1758, 1733, 1604, 1537, 1433, 1392, 1275, 1301, 1253, 1214, 1143, 1121, 1102, 1020, 993, 875, 772, 751, 722, 707, 681, 590 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.97 (1 H, dd, *J* 1.5, 0.9 Hz, pyr-H), 8.80 (1 H, dd, *J* 5.0, 0.9 Hz, pyr-H), 8.01 (1 H, dd, *J* 5.0, 1.5 Hz, pyr-H), 5.74 (2 H, s, CH_2-tet), 4.47 (2 H, q, *J* 7.1 Hz, CH_2), 4.19 (2 H, q, *J* 7.1 Hz, CH_2), 1.44 (3 H, t, *J* 7.1 Hz, CH_3), 1.19 (3 H, t, *J* 7.1 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 165.8 (C=O), 163.9 (C=O), 151.8 (CN_4), 150.0, 145.5, 139.6, 124.7, 123.5, 62.4 (OCH_2), 62.2 (OCH_2), 51.1 (CH_2-tet), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI): $[M+H]^+$, found 306.1195. $C_{13}H_{16}N_5O_4$ requires 306.1197.

Ethyl 2-(2-(2-ethoxy-2-oxoethyl)-2H-tetrazol-5-yl)isonicotinate (**3^2**)

White solid (0.72 g, 40%). m.p. 89-92 °C; ν_{max}(KBr) 3075, 2994, 2952, 1756, 1716, 1605, 1564, 1473, 1427, 1376, 1355, 1299, 1259, 1220, 1201, 1174, 1110, 1098, 1050, 1025, 886, 874, 783, 763, 682 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.94 (1 H, dd, *J* 4.9, 0.8 Hz, pyr-H), 8.80 (1 H, dd, *J* 1.6, 0.8 Hz, pyr-H), 7.98 (1 H, dd, *J* 4.9, 1.6 Hz, pyr-H), 5.54 (2 H, s, CH_2-tet), 4.47 (2 H, q, *J* 7.1 Hz, CH_2), 4.29 (2 H, q, *J* 7.1 Hz, CH_2), 1.45 (3 H, t, *J* 7.1 Hz, CH_3), 1.29 (3 H, t, *J* 7.1 Hz, CH_3; δ_C (75 MHz, $CDCl_3$) 164.7 (C=O), 164.7 (CN_4), 163.9 (C=O), 147.4, 139.1, 124.2, 121.8, 62.8 (OCH_2), 62.1 (OCH_2), 53.6 (CH_2-tet), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI): $[M+H]^+$, found 306.1197. $C_{13}H_{16}N_5O_4$ requires 306.1197.

Synthesis of 2-(1-(Carboxymethyl)-1H-tetrazol-5-yl)isonicotinic acid-(**4^1**)

Compound **3^{1}B** (0.30 g, 0.98 mmol) was dissolved in EtOH (20 mL). NaOH (0.20 mL, 10 M NaOH) was added to the solution and was heated to reflux overnight. The reaction mixture was concentrated under reduced pressure and the remaining residue was then dissolved in deionised H_2O (3 mL). 1 M HCl was added to the solution whilst stirring until precipitation commenced. The mixture was then allowed to stir at room temperature for 1 h, filtered and

the precipitate was washed with H_2O. White solid (0.18 g, 75%). m.p. 165-170 °C; ν_{max}(KBr) 3431, 3014, 2573, 1726, 1640, 1548, 1432, 1403, 1271, 1246, 1123, 1092, 912, 819, 783, 747, 730, 673, 546 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.94 (1 H, dd, *J* 4.9, 0.8 Hz, pyr-H), 8.64 (1 H, dd, *J* 1.5, 0.8 Hz, pyr-H), 8.02 (1 H, dd, *J* 4.9, 1.5 Hz, pyr-H), 5.75 (2 H, s, CH_2-tet); δ_C (75 MHz, $CDCl_3$) 167.8 (C=O), 165.1 (C=O), 151.7 (CN_4), 150.9, 144.8, 140.1, 124.7, 122.3, 50.9 (CH_2-tet); HRMS (ESI): $[M+H]^+$, found 250.0567. $C_9H_8N_5O_4$ requires 250.0571.

Synthesis of 2-(2-(Carboxymethyl)-2H-tetrazol-5-yl)isonicotinic-acid (**4²**)

Compound **3²B** (0.30 g, 0.98 mmol) was dissolved in EtOH (20 mL). NaOH (0.20 mL, 10 M NaOH) was added to the solution and was heated under reflux for 4 h. The reaction mixture was concentrated under reduced pressure and the remaining residue was then dissolved in deionised H_2O (3 mL). 1 M HCl was added to the solution whilst stirring until precipitation commenced. The mixture was then allowed to stir at room temperature for 1 h, filtered and the precipitate was washed with H_2O. White solid (0.16 g, 66%). m.p. 225-230 °C. IR (KBr): ν = 3421, 3026, 2901, 2595, 2508, 1725, 1708, 1615, 1565, 1474, 1416, 1396, 1372, 1286, 1261, 1232, 1199, 1178, 1118, 1095, 1004, 876, 856, 818, 761, 722, 666, 645 cm^{-1}. ^{1}H NMR (d_6-DMSO): δ = 8.95 (dd, 1 H, *J* = 4.9, 0.8 Hz, pyr-H), 8.52 (dd, 1 H, *J* = 1.5, 0.8 Hz, pyr-H), 7.98 (dd, 1 H, *J*= 4.9, 1.5 Hz, pyr-H), 5.80 (s, 2 H, CH_2-tet) ppm. ^{13}C NMR (d_6-DMSO): δ = 167.3 (C=O), 165.4 (C=O), 163.7 (CN_4), 151.4, 146.9, 139.6, 124.1, 121.0, 53.8 (CH_2-tet) ppm. ESI-HRMS: calcd. for $C_9H_8N_5O_4$ $[M+H]^+$ 250.0571, found 250.0559.

X-ray Structure Determination

Single crystal X-ray data collection, data reduction, structure solution and refinement are as described previously.[7] Selected crystallographic and structural information are available on the Cambridge Structural Database. Molecular and hydrogen bonding diagrams (Figure 2) were generated using ORTEP (with displacement ellipsoids drawn at the 30% probability level) and with atoms as their van der Waals spheres.[7] CCDC reference codes 1473138-1473142 and copies available, e-mail:deposit@ccdc.cam.ac.uk.

Acknowledgements

We are thankful to Maynooth University and to the Irish Research Council for financial assistance through the provision of a John & Pat Hume Fellowship and a Postgraduate Scholarship, respectively (US). JFG thanks Dublin City University for grants in aid of research.

References

1. (a) Cui, Y.; Yue, Y.; Qian, G.; Chen, B. *Chem. Rev*., **2012**, *112*, 1126; (b) Bétard, A.; Fischer, R. A. *Chem. Rev*., **2012**, *112*, 1055; (c) Wu, H.; Gong, Q.; Olson, D. H.; Li, J. *Chem. Rev*., **2012**, *112*, 836; (d) Horcajada, P.; Gref, R.; Baati, T.; Allan, P. K.; Maurin, G.; Couvreur, P.; Férey, G.; Morris, R. E.; Serre, C. *Chem. Rev*., **2012**, *112*, 1232; (e) Kreno, L. E.; Leong, K.; Farha, O. K.; Allendorf, M.; Van Duyne, R. P.; Hupp, J. T. *Chem. Rev*., **2012**, *112*, 1105, (f) Petit, C.; Bandosz, T. J. *Dalton Trans*., **2012**, *41*, 4027; (g) Allan, P. K.; Wheatley, P. S.; Aldous, D.; Mohideen, M. I.; Tang, C.; Hriljac, J. A.; Megson, I. L.; Chapman, K. W.; De Weireld, G.; Vaesen, S.; Morris, R. E. *Dalton Trans*., **2012**, *41*, 4060; (h) Cirujano, F. G.; Llabrés i Xamena, F. X.; Corma, A. *Dalton Trans*., **2012**, *41*, 4249.
2. Liu, G.-Z.; Xin, L.-Y.; Wang, L.-Y. *CrystEngComm*, **2011**, *13*, 3013.
3. See, for example, (a) Ma, N.; Guo, W.-Y.; Song, H.-H.; Yu, H.-T. *J. Solid State Chem*., **2016**, *233*, 381; (b) Li, L.; Liu, C.-B.; Yang, G.-S.; Xiong, Z.-Q.; Liu, H.; Wen, H.-L. *J. Solid State Chem*., **2015**, *231*, 70; (c) Datta, A.; Massera, C.; Clegg, J. K.; Aromi, G.; Aguila, D.; Huang, J.-H.; Chuang, S.-J. *CrystEngComm*., **2015**, *17*, 4502; (d) Zhao, Y.; Chang, X.-H.; Liu, G.-Z.; Ma, L.-F.; Wang, L.-Y. *Cryst. Growth Des*., **2015**, *15*, 966; (e) Liu, B.; Wei, L.; Li, N.-N.; Wu, W.-P.; Miao, H.; Wang, Y.-Y.; Shi, Q.-Z. *Cryst. Growth Des*., **2014**, *14*, 1110; (f) Chandrasekhar, V.; Mohapatra, C. *Cryst. Growth Des*., **2013**, *13*, 4655.
4. Wang, Y.; Shen, S.-Q.; Zhou, J.-H.; Wang, T.; Wang, S.-N.; Liu, G.-X. *Inorg. Chem. Commun.*, **2013**, *30*, 5.
5. (a) Burrows, A. D.; Harrington, R. W.; Mahon, M. F.; Teat, S. J. *Eur. J. Inorg. Chem.*, **2003**, 766; (b) Burrows, A. D.; Harrington, R. W.; Mahon, M. F.; Price, C. E. *Dalton Trans.*, **2000**, 3845; (c) Shyu, E.; Braverman, M. A.; Supkowski, R. M.; LaDuca, R. L. *Inorg. Chim. Acta*, **2009**, *362*, 2283; (d) Braverman, M. A.; Staples, R. J.; Supkowski, R. M.; LaDuca, R. L. *Polyhedron*, **2008**, *27*, 2291.

6. (a) Sheridan, U.; McGinley, J.; Gallagher, J. F.; Bjerrum, M. J.; Fleming, A.; Kelleher, F. *Inorg. Chim. Acta*, **2014**, *421*, 200; (b) Sheridan, U.; Gallagher, J. F.; Philippidis, A.; McGinley, J. *Inorg. Chim. Acta*, **2015**, *432*, 50; (c) Sabatini, J. J.; Moretti, J. D. *Chem. Eur. J.*, **2013**, *19*, 12839; (d) Malik, M.; Wani, M.; Al-Thabaiti, S.; Shiekh, R. *J. Incl. Phenom. Macrocycl. Chem.*, **2014**, *78*, 15.

7. (a) Oxford Diffraction Ltd. ABSFAC and CrysAlisPro CCD/RED, *Version 1.171.33.55*, Oxford Diffraction, Abingdon, Oxfordshire, U.K; (b) Sheldrick, G. M. *Acta Crystallogr. Sect. A*, **2008**, *64*, 11; (c) McArdle, P. *J. Appl. Cryst.*, **1995**, *28*, 65; (d) Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P. A. *J. Appl. Cryst*., **2008**, *41*, 466.

8. (a) Mocilac, P.; Tallon, M.; Lough, A. J.; Gallagher, J. F. *CrystEngComm*., **2010**, *12*, 3080; (b) Mocilac, P.; Donnelly, K.; Gallagher, J. F. *Acta Crystallogr*., **2012**, *B68*, 189.

9. Spek, A. L. *Acta Crystallogr*., **2009**, *D65*, 148.

10. Arnaud-Neu, F.; Barrett, G.; Cremin, S.; Deasy, M.; Ferguson, G.; Harris, S. J.; Lough, A. J.; Guerra, L.; McKervey, M. A.; Schwing-Weill, M. J.; Schwinte, P. *J. Chem. Soc. Perkin Trans. 2*, **1992**, *7*, 1119.

11. Sheridan, U.; Gallagher, J. F.; Fadda, E.; Bjerrum, M. J.; McGinley, J. *Supramol. Chem*., **2016**, DOI:10.1080/10610278.2015.1123261.

12. Huo, Z.; Kosugi, T.; Yamamoto, Y. *Tetrahedron Lett.*, **2008**, *49*, 4369.

13. Sato, N.; Ando, M.; Ishikawa, S.; Jitsuoka, M.; Nagai, K.; Takahashi, H.; Sakuraba, A.; Tsuge, H.; Kitazawa, H.; Iwaasa, H.; Mashiko, S.; Gomori, A.; Moriya, R.; Fujino, N.; Ohe, T.; Ishihara, A.; Kanatani, A.; Fukami, T. *J. Med. Chem.*, **2009**, *52*, 3385.

14. Sakamoto, T.; Kaneda, S.; Nishimura, S.; Yamanaka, H. *Chem. Pharm. Bull.*, **1985**, *33*, 565.

15. (a) Sheridan, U.; McGinley, J.; Gallagher, J. F.; Fleming, A.; Kelleher, F. *Polyhedron*, **2013**, *59*, 8; (b) Bond, A. D.; Fleming, A.; Gaire, J.; Kelleher, F.; McGinley, J.; McKee, V.; Sheridan, U. *Polyhedron*, **2012**, *33*, 289.

16. (a) Butler, R. N.; Fleming, A. F. M. *J. Heterocycl. Chem*., **1997**, *34*, 691; (b) Bethel, P. A.; Hill, M. S.; Mahon, M. F.; Molloy, K. C. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 3507; (c) Fleming, A.; Kelleher, F.; Mahon, M. F.; McGinley, J.; Prajapati, V. *Tetrahedron*, **2005**, *61*, 7002; (d) Bond, A. D.; Fleming, A.; Gaire, J.; Kelleher, F.;

McGinley, J.; McKee, V. *Tetrahedron*, **2009**, *65*, 7942; (e) Fleming, A.; Gaire, J.; Kelleher, F.; McGinley, J.; McKee, V. *Tetrahedron*, **2011**, *67*, 3260.

17. Gallagher, J. F.; Alley, S.; Brosnan, M.; Lough, A. J. *Acta Cryst*., **2010**, *B66*, 196.
18. Castañeda, F.; Silva, P.; Bunton, C. A.; Garland, M. T.; Baggio, R. *Acta Cryst*., **2008**, *C64*, o405.
19. Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond*, Oxford University Press, **1999**, 86.
20. (a) Allen, F. H.; Raithby, P. R.; Shields, G. P.; Taylor, R. *Chem. Comm*., **1998**, 1043; (b) Allen, F. H. *Acta Cryst. B*., **2002**, *B58*, 380.
21. Clayden, J.; Greeves, N.; Warren, S. *Organic Chemistry*, Oxford University Press, 2nd Edition, **2012**, 209.
22. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds: Applications in Coordination, Organometallic, and Bioinorganic Chemistry*, sixth edition, Wiley-Blackwell, **2009**.
23. Ferguson, G.; Gallagher, J. F.; McAlees, A. J. *Acta Cryst*., **1995**, *C51*, 454.
24. Vishweshwar, P.; Nangia, A.; Lynch, V. M. *J. Org. Chem*., **2002**, *67*, 556.
25. See, for example, (a) Ayhan, O.; Malaestean, I. L.; Ellern, A.; van Leusen, J.; Baca, S. G.; Kögerler, P. *Cryst. Growth Des*., **2014**, *14*, 3541; (b) Henke, S.; Fischer, R. A. *J. Am. Chem. Soc*., **2011**, *133*, 2064.
26. Butler, R. N. in Comprehensive Heterocyclic Chemistry II (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Permagon, Oxford, **1996**, *4*, pp. 621.
27. Yin, J.; Xiang, B.; Huffman, M. A.; Raab, C. E.; Davies, I. W. *J. Org. Chem.*, **2007**, *72*, 4554.
28. Duric, S.; Tzschucke, C. C. *Org. Lett.*, **2011**, *13*, 2310.