C–H group acidity and the nature of C–H···N interactions: crystal structural analysis of pyrazine and methyl substituted pyrazines

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Received (in Montpellier, France) 3rd March 2000, Accepted 30th March 2000
Published on the Web 18th May 2000

Crystal structures of methyl-, 2,3-, 2,5- and 2,6-dimethyl-, and trimethylpyrazine (**2**–**6**) have been determined by X-ray diffraction analysis. Four of these compounds (**2**–**4** and **6**) are liquids and their single crystals have been grown *in situ* on the diffractometer using a miniature zone melting procedure. These structures are analysed together with those of pyrazine (**1**) and tetramethylpyrazine (**7**) in the context of C–H···N interactions. Compounds **1**–**7** were chosen because they contain only C, H and N atoms, and also C–H groups of variable acidity. This facilitates the comparison of C–H···N geometries with respect to the C–H group acidity. Compounds **1** and **2** are dominated by sp^2 C–H groups in their molecules and their supramolecular structures are generated by sp^2 C–H···N. On the other hand the domination of sp^3 C–H groups at the molecular level in **6** and **7** results in crystal structures that are governed by sp^3 C–H···N. A balance of sp^2 and sp^3 C–H groups in the dimethyl derivatives **3**–**5** leads to a situation where both kinds of C–H groups play a structure directing role. While the sp^2 C–H groups form C–H···N, the sp^3 C–H groups are involved in C–H···π interactions. Thus the C–H group interactions follow a property unique to hydrogen bonds—stronger donors interact with stronger acceptors while weaker donors approaching weaker acceptors. Inter-structural comparison revealed that H···N distances decrease with increasing C–H acidity and therefore C–H···N interactions could be considered as weak hydrogen bonds.

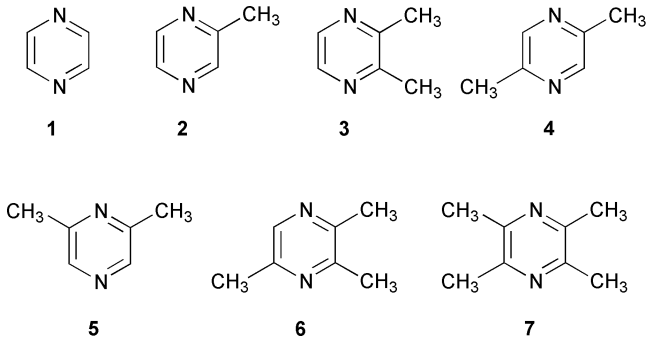
Hydrogen bonds, typically denoted as X–H···Y in structural chemistry and biology, exist (*a*) when the electronegativity of X is relatively higher than H and (*b*) when Y shares a lone pair of electrons with a partially positive H atom.[1] The groups X–H and Y are called the hydrogen bond donor and acceptor, respectively. This landmark concept, laid down as early as 1939,[2] led to an enormous development of chemistry and biology alike.[3] Many of the initial studies were restricted to X and Y being equal to O or N. These X–H···Y bonds (where X, Y = O or N) are today referred to as conventional or strong hydrogen bonds. As the subject progressed, weakly polar C–H groups (electronegativity of C is only slightly higher than H) were also found to participate in hydrogen bonding.[4] Even the π systems of aromatic rings and triple bonds were realised to act as hydrogen bond acceptors.[5] These bonds involving weak donors and/or weak acceptors are generally called non-conventional or weak hydrogen bonds.[6]

Today a hydrogen bond is recognised not by its definition but by its spectroscopic, structural or quantum chemical characteristics. For a strong hydrogen bond the difference in the stretching frequencies of the X–H bond in a free molecule and in a hydrogen bonded supermolecule is large enough that it can be easily and accurately detected. As the interaction becomes weaker this difference in the vibrational frequency becomes smaller and therefore structural analysis assumes greater significance in the characterisation of weak hydrogen bonds. Structural studies typically involve single crystal X-ray or neutron diffraction analyses and provide X–H···Y geometries *viz*. X···Y and H···Y distances and X–H···Y angles.

The C–H···O interaction is the most widely investigated weak hydrogen bond. Numerous studies[6,7] that have dealt with this interaction have proved, among other things, that (*a*) it involves an electrostatic attraction between the C–H group and O atom, (*b*) it operates over a long distance range, even beyond the van der Waals limit, (*c*) it is directional, and (*d*) it contributes to the stabilisation of supramolecular species, which it holds together. The fact that C–H groups are prevalent in organic and biological compounds has spurred the widespread interest in, and extensive investigations into the C–H···O hydrogen bond. In contrast, the conceptually very similar C–H···N interaction has been scarcely studied.[8] Very often the properties of C–H···O hydrogen bonds are assigned to C–H···N interactions.[4b,6]

The nature of the C–H···N interaction has been the subject of recent controversy. Imposing stringent limits on the values of H···N distances and C–H···N angles, it was claimed in a recent paper that many of the reported C–H···N hydrogen bonds are classical van der Waals contacts.[9] A subsequent statistical analysis,[10] using the Cambridge Structural Database (CSD), of these interactions has shown that about 1000 contacts exist in the reported structures with H···N distances shorter than 2.45 Å (van der Waals sum 2.75 Å)[11] and with a mean C–H···N angle of 155°.[12] Statistical approaches to the properties of C–H···N interactions, analogous to those of C–H···O hydrogen bonds, are difficult because of the dearth of available data.[13] We believe that an experimental approach to investigate the properties of C–H···N interactions would be very useful and in the present work we have adopted this approach.

To study the nature of C–H···N interactions, compounds **1**–**7** (Scheme 1) have been chosen. Independent crystal structure determinations of **1** and **7** exist in the literature.[14,15] We determined the crystal structures of **2**–**6**,[16] and these are discussed along with those of **1** and **7** in this article. There are several reasons for the selection of these compounds. (*a*) They are chemically homogeneous. (*b*) They contain C, H and N atoms only and therefore the possibility of competition with other stronger interactions is avoided. (*c*) They have the same molecular core with two N-acceptors in a fixed geometry. (*d*) They contain C–H donor groups with variable acidity (aromatic and aliphatic), in variable geometries and in vari-



Scheme 1 Compounds analysed in the present work.

able proportions, offering a greater scope to study the effect of C–H acidity on the nature of C–H···N interactions. It should be noted that C–H···π and π···π interactions are also possible in the structures of **1**–**7**.

Experimental

Compounds **2**–**6** were commercially available and used in the crystallisation as received. Single crystals of **5** were obtained when a methanol solution was slowly evaporated. Because compounds **2**, **3**, **4** and **6** are liquids at room temperature, the miniature zone melting technique developed in our laboratory was used to grow their single crystals directly on the diffractometer.[17] Differential scanning calorimetry experiments were carried out on **2**–**6** and no phase transitions were observed. The melting points were recorded. The diffractometer was equipped with a cooling device and a fine focussed CO_2 IR laser set-up. The intensity and position of the laser were computer controlled. In a typical crystal growth experiment, the liquid sample was loaded into a thin-walled quartz capillary (0.3 mm diameter) and mounted on the goniometer. The sample was slowly cooled below its melting point such that it became polycrystalline. The laser beam was then shone on the bottom of the capillary with an intensity sufficient to melt a tiny portion of the sample. The beam was then scanned along the length of the capillary to turn the polycrystalline sample into a single crystal. The quality of the crystal obtained was checked by means of X-ray rotation photographs. Many cycles of scanning and different temperature and laser intensity conditions were attempted before a suitable single crystal was obtained. The optimal growing conditions (temperature, scan speed and laser intensity) vary from sample to sample and were found during the experiments. Once the suitable single crystal was grown it was slowly cooled down to the temperature of data collection.

The X-ray data for **2**, **3**, **4** and **6** were collected on a Nicolet R3 diffractometer, and for **5** on a Bruker SMART area detector diffractometer, using Mo-Kα radiation. The structure solution and refinements were carried out using the SHELXS-86[18] and SHELXL-97[19] programs, respectively. All non-H atoms were refined anisotropically. All the H atoms could be located from difference Fourier maps but for consistency they were generated using the geometrical routines in the refinement program. They were isotropically refined with the riding model on idealised geometries. The salient crystallographic details for **2**–**6** are given in Table 1.

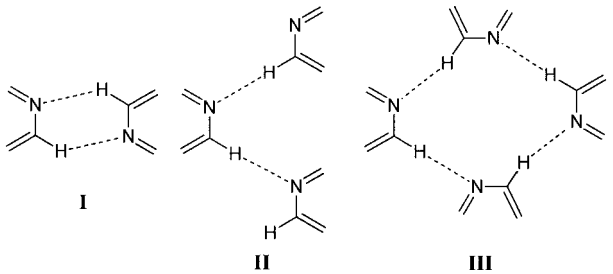
CCDC reference number 440/181. See http://www.rsc.org/suppdata/nj/b0/b001843k/ for crystallographic files in .cif format.

Results and discussion

The emphasis of the present work is on the structural attributes of C–H···N interactions and the role played by them in the crystal structures of **1**–**7**. From the structural analysis of these compounds we hope to find various repeating interaction patterns, the supramolecular synthons.[20] Scheme 2 shows some of the C–H···N based synthons observed in **1**–**7**. Synthons **I** and **II** resemble the dimer and catemer motifs of carboxylic acid groups[21] and we shall refer to these as dimer and catemer in the following sections. We note that in some cases the catemer synthon exists in a helical variation and this will be termed helical catemer.

It is important to distinguish the aromatic and aliphatic (methyl) C–H groups in the structures of **1**–**7** as we intend to analyse the nature of C–H···N interactions with respect to C–H group acidity. In the discussion that follows we refer to aromatic and aliphatic (methyl) C–H groups as sp^2 C–H and sp^3 C–H groups, respectively.

Various intermolecular interactions found in the structures of **1**–**7** are collected in Table 2. For C–H···N and C–H···π interactions the contacts with H···N/π distances shorter than 3.0 Å and C–H···N/π angles greater than 110° are listed. These interactions, described in the following sections, are



Scheme 2 C–H···N based supramolecular synthons.

Table 1 Crystal data and measurement details for **2**–**6**

	2	**3**	**4**	**5**	**6**
Emp. formula	$C_5H_6N_2$	$C_6H_8N_2$	$C_6H_8N_2$	$C_6H_8N_2$	$C_7H_{10}N_2$
Formula wt.	94.12	108.14	108.14	108.14	122.17
T/K	123	180	180	180	180
Crystal system	Tetragonal	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$I\bar{4}$	$P2_1/c$	$P2_1/n$	$P2_1/c$	$P2_1/c$
a/Å	13.725(2)	7.811(1)	5.702(1)	7.557(1)	9.144(2)
b/Å		6.551(1)	5.048(2)	10.855(1)	10.243(2)
c/Å	10.859(2)	12.164(1)	10.664(2)	7.445(1)	15.212(3)
β/°		108.61(1)	104.55(2)	90.53(1)	95.55 (1)
Z	16	4	2	4	8
U/Å^3	204.56(8)	589.9(2)	297.1(1)	610.7(2)	1418.1(4)
Total reflect.	1504	1786	540	5124	3748
Indep. reflect.	1338	1711	513	1431	2491
R_{int}	0.019	0.068	0.021	0.053	0.018
R_1	0.030	0.041	0.032	0.081	0.049
wR_2	0.080	0.112	0.083	0.206	0.116
μ/mm^{-1}	0.08	0.08	0.08	0.07	0.07

Table 2 Geometrical parameters for various intermolecular interactions in **1**–**7**

Compound	Interaction	H···N(π)/Å[a]	C···N(π)/Å	C–H···N(π)/°	*M*···N···H/°
1	sp^2 C–H···N	2.50	3.485	152	143
2	sp^2 C–H···N	2.44	3.445	153	161
		2.52	3.532	156	158
		2.56	3.607	163	160
		2.66	3.697	161	132
		2.69	3.712	156	132
		2.72	3.705	152	135
	sp^3 C–H···N	2.66	3.521	136	148
		2.80	3.832	160	142
		2.98	3.912	145	132
3	sp^2 C–H···N	2.61	3.468	136	129
		2.90	3.871	150	154
	sp^3 C–H···N	2.83	3.830	154	120
	sp^3 C–H···π	2.70	3.696	142	
4	sp^2 C–H···N	2.59	3.605	157	135
	sp^3 C–H···N	2.83	3.825	153	153
	sp^3 C–H···π	2.82	3.811	152	
5	sp^2 C–H···N	2.56	3.637	173	172
		2.58	3.570	151	147
	sp^3 C–H···N	2.83	3.908	176	140
		2.94	3.764	133	126
	sp^3 C–H···π	2.72	3.554	134	
6	sp^2 C–H···N	2.85	3.785	144	168
	sp^3 C–H···N	2.60	3.662	167	130
		2.63	3.679	164	130
		2.66	3.723	167	168
		2.67	3.731	166	173
		2.70	3.740	162	128
		2.75	3.764	156	137
		2.81	3.823	156	126
		2.95	3.983	159	129
		2.97	4.030	165	131
7	sp^3 C–H···N	2.60	3.645	163	130
		2.70	3.751	165	170
		2.75	3.800	164	129

[a] The C–H bond lengths are normalised to 1.083 Å.

referred to on the basis of H···N/π distances. If a C–H group approaches an aromatic ring in a direction perpendicular (or nearly perpendicular) to the ring plane then the interaction is more likely of a C–H···π type than a C–H···N one. In order to avoid such a conflict in distinguishing the interaction type, only those C–H···N contacts with *M*···N···H (*M* is the midpoint on the vector joining the two N atoms of a ring) angle greater than 120° are considered.

Helical sp^2 C–H···N catemers in pyrazine (1)

Compound **1** crystallises in the space group *Pmnn* ($Z = 2$)[14b] and contains only one symmetry independent sp^2 C–H group. Fig. 1 shows the packing pattern of **1**. Each molecule is connected to eight others through helical sp^2 C–H···N (2.50 Å) catemers, which form a three-dimensional network. All the sp^2 C–H groups are involved in C–H···N bridges, and each Natom is bifurcated between two H atoms. Translated molecules along [001] are held together by π-stacking (3.43/3.73 Å)[22] interactions between aromatic rings [Fig. 1(*b*)].

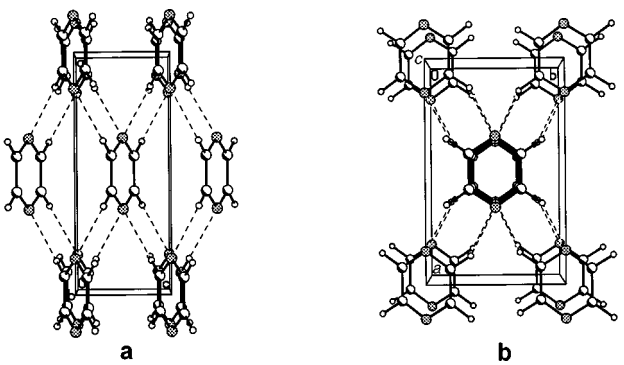


Fig. 1 Crystal structure of **1** viewed down [010] and [001]. Notice the helical sp^2 C–H···N catemers in (*a*) and π stacking in (*b*). In all the figures C–H···N interactions are drawn as dashed lines.

In compound **1** all the four H atoms are chemically equivalent and replacing any one of these by a methyl group results in compound **2**, which contains both sp^2 and sp^3 C–H groups.

Columnar structures from sp^2 C–H···N tetramers in methylpyrazine (2)

The crystals of **2** were grown *in situ* on the diffractometer and exhibited merohedral twinning.[23] Compound **2** crystallises in the space group $I\bar{4}$ with two molecules in the asymmetric unit. These are termed **A** and **B**. The structure of **2** is displayed in Fig. 2(*a*) wherein **A** and **B** molecules are drawn with open and cross-hatched atoms, respectively. Molecules **A** and **B** may be said to form crystallographically independent columns running respectively along 0, 0, *z* and 0, $\frac{1}{2}$, *z*. The intermolecular arrangement in these independent columns is similar. To understand the C–H···N patterns in these columns it is convenient to distinguish the three chemically (and crystallographically) different aromatic H atoms. These H atoms are numbered according to their position on the ring as shown in Scheme 3.

In each column the molecules are connected with two kinds of cyclic sp^2 C–H···N tetramers (**III**, Scheme 2). Fig. 2(*b*) shows the tetrameric patterns in a column. One of the tetramers is formed by contacts between H3/H13 and N4/N14 (2.66, 2.69 Å) and the other by H6/H16 and N1/N11 (2.44, 2.52 Å). Each molecule is involved in both kinds of tetrameric loops, which alternate along the column. Within each column the packing is also assisted by π-stacking (**A**: 3.47/3.58 Å; **B**: 3.47/3.69 Å) between molecules that are related by 2-fold axes.

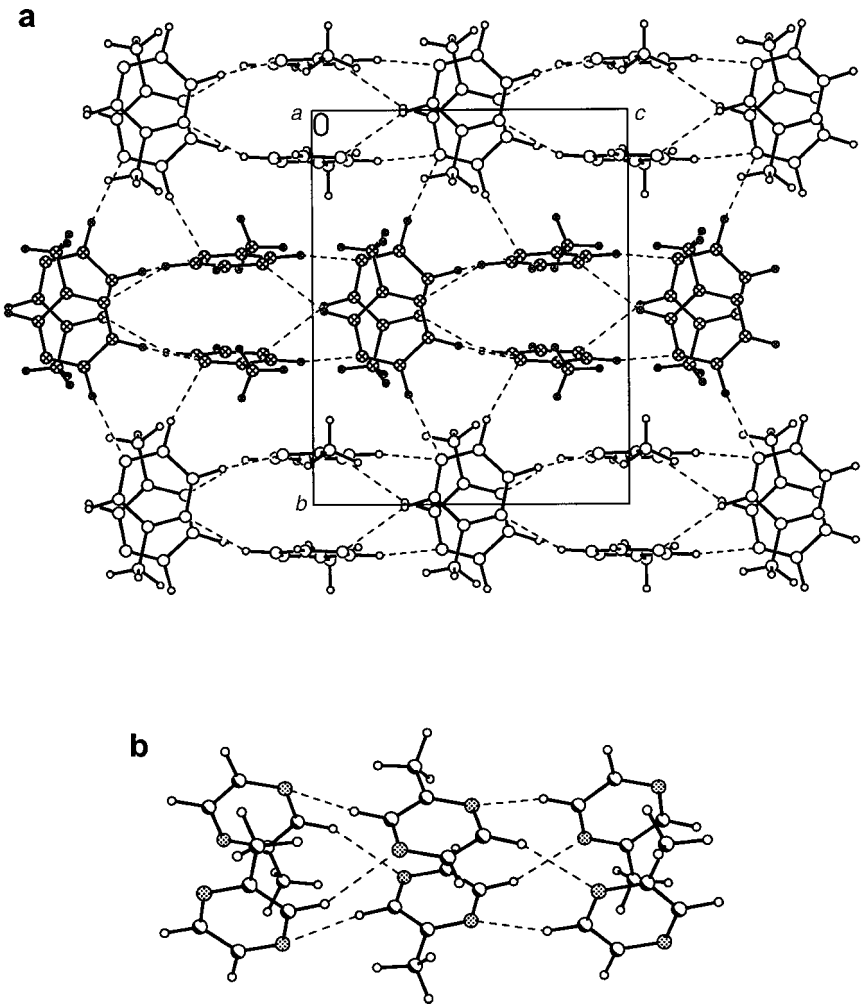


Fig. 2 (*a*) Crystal structure of **2** viewed down [100]. Notice the sp^2 C–H···N tetramers in both independent columns and intercolumn sp^2 C–H···N interactions. (*b*) A perspective view showing the tetrameric patterns in one of the independent columns.

All the sp^2 C–H···N interactions within the columns are of **A**-to-**A** or **B**-to-**B** type. The sp^2 C–H···N interactions also interconnect the columns and these are of **A**-to-**B** (H5···N11, 2.72 Å) and **B**-to-**A** (H15···N4, 2.56 Å) type. Thus, all the sp^2 C–H groups are effectively involved in the networking of molecules. In addition to sp^2 C–H···N, some sp^3 C–H···N contacts are also observed but these are either longer or bent (Table 2).

The transition from a mono- to a dimethyl derivative of pyrazine would lead to three possibilities (**3**, **4** and **5**) because the three aromatic H atoms in **2** are chemically different. Compounds **3**, **4** and **5** possess the same composition but have different geometries. The H atom numbering of **3**–**5** shown in Scheme 3 will be used in the description of packing patterns in these structures.

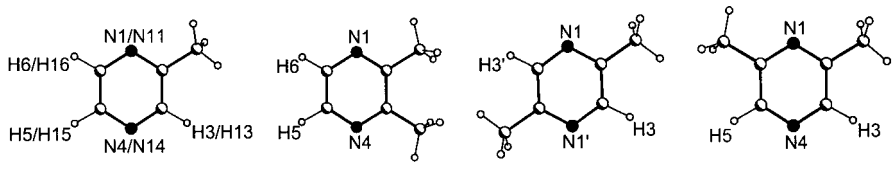
sp^2 C–H···N dimers and catemers, and sp^3 C–H···π dimers in 2,3-dimethylpyrazine (3)

Compound **3** crystallises in the space group $P2_1/c$ ($Z = 4$) and the two sp^2 C–H groups are crystallographically different. Both these C–H groups are involved in C–H···N interactions. While H6 generates a catemer along the 2_1-axis [2.61 Å, Fig. 3(*a*)], inversion related dimers are formed by H5 [2.90 Å, Fig. 3(*b*)]. Thus each molecule of **3** is involved in both synthons **I** and **II**, resulting in a three-dimensional C–H···N assembly. For clarity, however, the patterns including the dimer and catemer synthons are shown separately in Figs. 3(*a*) and 3(*b*).

Fig. 3b illustrates another important structural feature of **3**. One of the methyl groups interacts with the aromatic ring through sp^3 C–H···π interactions (2.70 Å). These sp^3 C–H···π interactions extend to a dimeric motif. Within the structural series **1**–**7** the acceptor capabilities of the aromatic ring are revealed for the first time in **3**. Additionally, ring stacking (3.40/3.58 Å) and methyl–methyl close packing[24] (C···C, 3.61 Å) are seen in the structure of **3** [Fig. 3(*b*)].

Two-dimensional sp^2 C–H···N networks and sp^3 C–H···π dimers in 2,5-dimethylpyrazine (4)

Compound **4** has a molecular centrosymmetry and crystallises in the space group $P2_1/n$ with half a molecule in the asym-



Scheme 3 Atom numbering in **2**–**5**. H3/H13 *etc.*, in **2** correspond to two symmetry independent molecules. Symmetry related atoms are numbered with a prime in **4**.

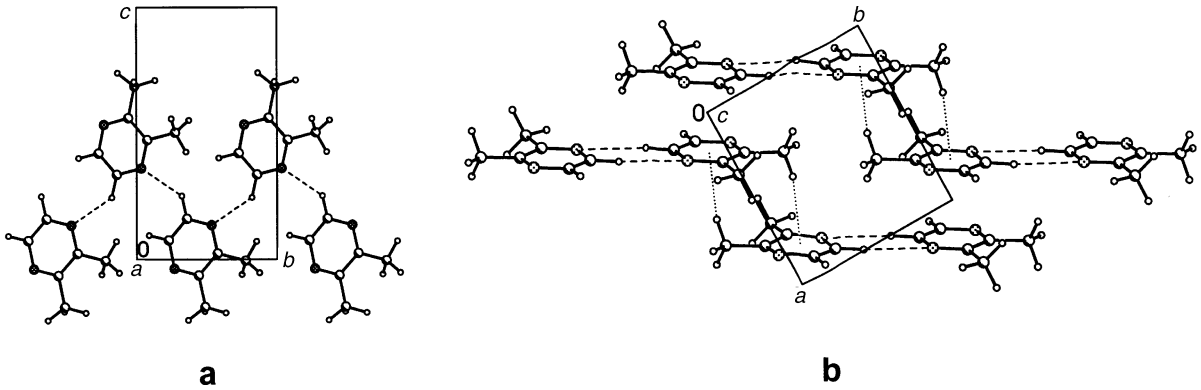


Fig. 3 Catemer (*a*) and dimer (*b*) sp^2 C–H···N synthons in **3**. Notice that the sp^2 C–H groups involved in catemer and dimer synthons are crystallographically different. Notice also the sp^3 C–H···π dimers, ring stacking and methyl–methyl close packing in (*b*). In this and the following figures C–H···π interactions are drawn as dotted lines.

metric unit. The two symmetry related sp^2 C–H groups (H3 and H3′) are involved in helical C–H···N catemer synthons and generate two-dimensional networks (Fig. 4). Molecules are inclined with respect to the mean plane of the network to facilitate the sp^3 C–H···π (2.82 Å) interactions between methyl groups and aromatic rings. Again, these sp^3 C–H···π interactions form dimeric motifs that run in a consecutive manner parallel to the catemeric sp^2 C–H···N chains (Fig. 4). Methyl–methyl close packing (C···C, 3.66 Å) predominates the inter-network assembly.

sp^2 C–H···N mediated flat layers and interlayer sp^3 C–H···π interactions in 2,6-dimethylpyrazine (5)

The structure of **5** ($P2_1/c$, $Z = 4$) constitutes C–H···N mediated flat layers as shown in Fig. 5(*a*). The two sp^2 C–H groups in **5** are crystallographically distinct and both form C–H···N interactions. Inversion related molecules are linked through sp^2 C–H···N synthon **I** (H3···N4, 2.58 Å) to form dimers. Adjacent dimers, which are related by a 2_1-axis, are connected with sp^2 C–H···N interactions (H5···N1, 2.56 Å). This sp^2 C–H···N interaction is accompanied by a longer sp^3 C–H···N interaction [2.83 Å, not shown in Fig. 5(*a*)] connecting adjacent dimers. Within the flat layers shown in Fig. 5(*a*) methyl–methyl close packing (C···C, 3.74 Å) interactions fill up the cavities generated by C–H···N networking. As in **3** and **4** the methyl groups participate in sp^3 C–H···π interactions and govern the interlayer packing [Fig. 5(*b*)].

sp^3 C–H···N interactions in trimethylpyrazine (6)

Compound **6** is the only possible trimethyl derivative of pyrazine. It crystallises in the space group $P2_1/c$ with two symmetry independent molecules. These are referred to as **C** and **D**, and in Fig. 6 they are drawn with open and cross-hatched atoms, respectively. In both independent molecules the H atoms of one of the methyl groups are disordered over two positions. For clarity only one of the possible positions is shown in Fig. 6. Each independent molecule forms a stacked diad with an inversion related neighbour (stacking parameters: **C** = 3.47/3.75 Å; **D** = 3.54/3.75 Å). Stacked diads of **C** and **D** are linked to one another through a large number of C–H···N interactions leading to a three-dimensional assembly. Fig. 6 shows the structure of **6** parallel to (011). It is of great importance to note that the C–H···N network is generated mainly by sp^3 C–H groups. From Table 2 it may be seen that only the sp^2 C–H group of the **D** molecule forms a C–H···N contact. On the other hand the sp^3 C–H groups of

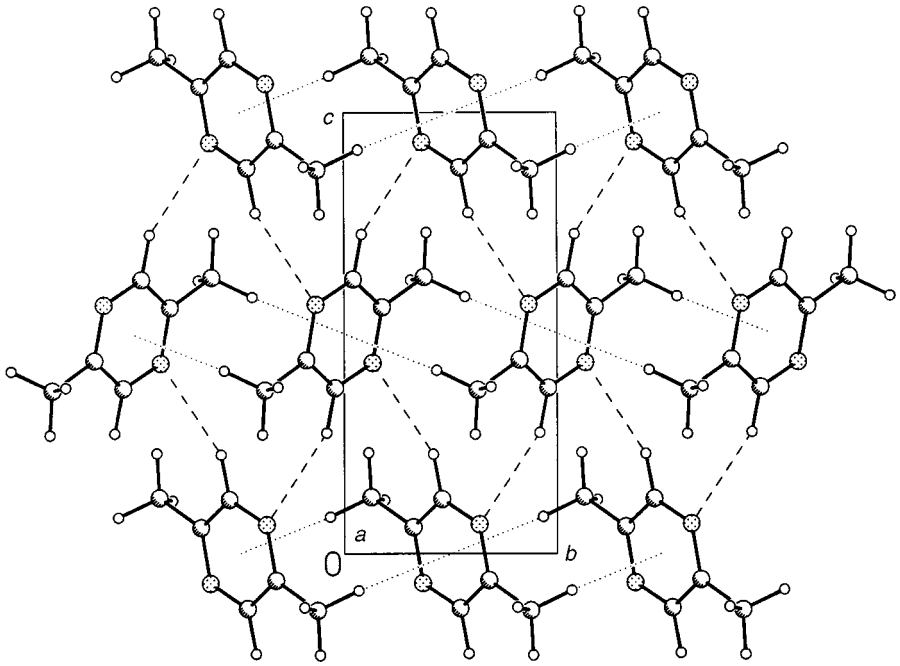


Fig. 4 sp^2 C–H···N networks and sp^3 C–H···π dimers in the crystal structure of **4**.

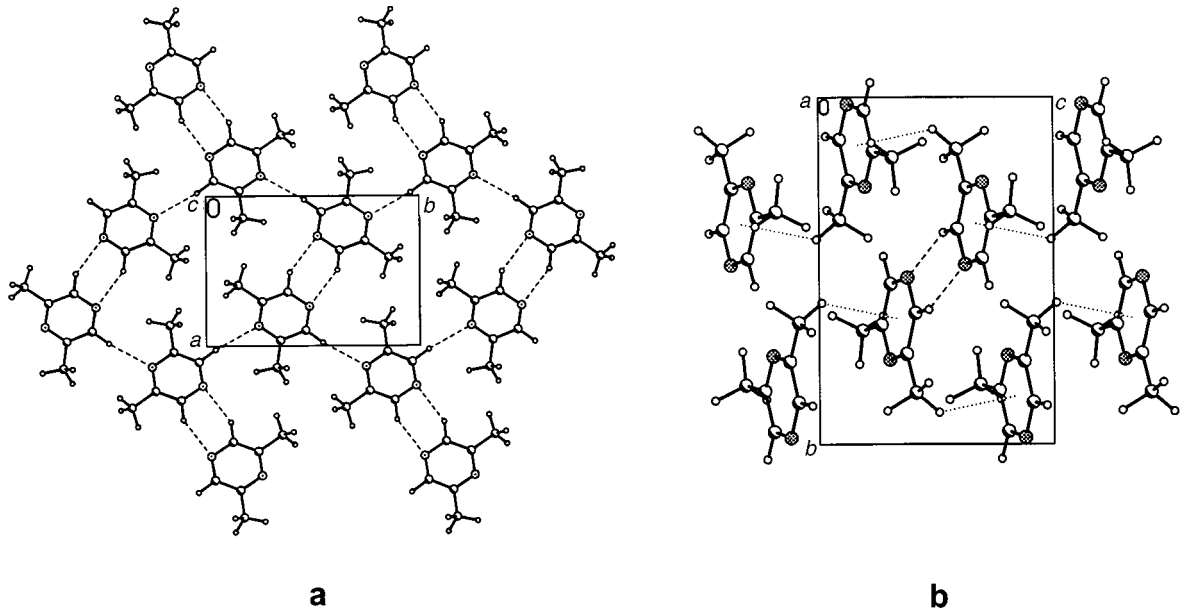


Fig. 5 Crystal structure of **5**. (*a*) View down [001] showing the flat layers generated by sp^2 C–H···N interactions. Notice the dimer synthons and methyl–methyl close packing. (*b*) View down [100] to show the interlayer sp^3 C–H···π interactions.

both **C** and **D** molecules participate in C–H···N interactions. Also important is the fact that the C–H···N interactions of sp^3 C–H groups are shorter and more linear than that of the sp^2 C–H group (Table 2). All the C–H···N interactions are of **C**-to-**D** or **D**-to-**C** type, and no C–H···π interactions are seen.

sp^3 C–H···N catemers in tetramethylpyrazine (7)

The tetramethyl derivative **7** contains only sp^3 C–H groups. The structure (*Pbca*, $Z = 4$)[15b] is built from sp^3 C–H···N (2.70 Å) mediated two-dimensional networks (Fig. 7). Because the molecules are positioned on inversion centres, the four chemically equivalent methyl groups are separated into two crystallographically distinct pairs. It may be seen from Fig. 7 that while one of these pairs is involved in sp^3 C–H···N interactions, the other participates in methyl–methyl close packing (C···C, 3.99 Å). The latter pair of methyl groups forms C–H···N contacts within (2.60 Å, not shown in Fig. 7)[25] and between (2.75 Å) the networks. None of the methyl groups are involved in C–H···π interactions.

Comparison of Fig. 4 and 7 reveals a striking similarity between the two-dimensional C–H···N networks in **4** and **7**. The sp^3 C–H···N pattern in **7** may now be viewed as an extended variation of catemer synthon **II** made up of sp^2 C–H···N interactions. In other words, the role played by the sp^3 C–H groups in the networks of **7** is very similar to that played by the sp^2 C–H groups in the structure of **4**.

Nature of C–H···N interactions

Independent structural analysis of **1**–**7** as described in previous sections led to the identification of various intermolecular interactions present in these structures. In this section the structures of **1**–**7** are compared in order to explore the characteristics of C–H group interactions. In **1**, all the C–H donors are of the sp^2 type and all of these contribute to the crystal packing through C–H···N interactions. Both sp^2 and sp^3

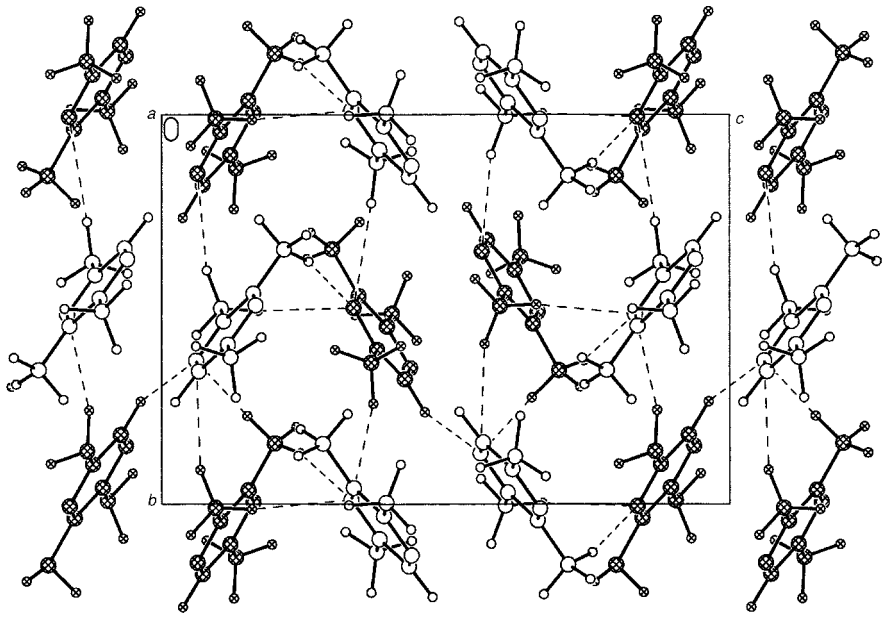


Fig. 6 View down [100] showing a two-dimensional cut-out of the crystal structure of **6**. Notice the stacked diads of independent molecules and a large number of interdiad C–H···N interactions.

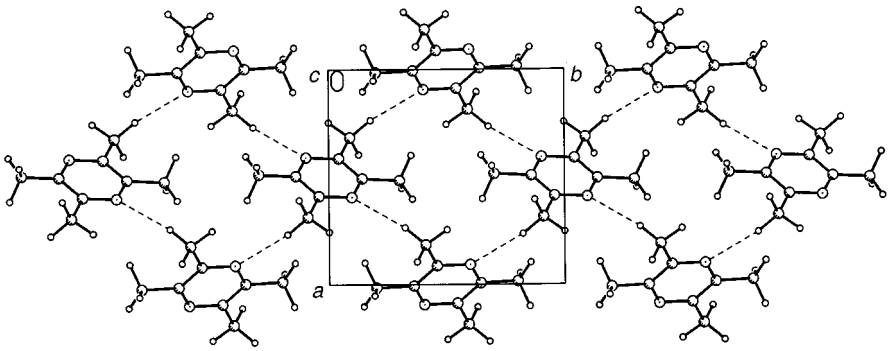


Fig. 7 sp^3 C–H···N mediated two-dimensional networks in the crystal structure of **7**. Compare this with Fig. 4 and notice the similarity to sp^2 C–H···N networks in **4**.

C–H donors are present in the monomethyl derivative **2**. While the sp^2 C–H groups play a crucial role in the structure of **2** and stabilise it in great part through C–H···N interactions, the role played by the sp^3 C–H groups is only supportive. There is no doubt that the sp^2 C–H groups are more acidic than their sp^3 counterparts. The greater acidity of sp^2 C–H groups confers greater strength to the interactions formed by them. It follows quite naturally that sp^2 C–H···N are the operative interactions in **2**.

In each of the dimethyl derivatives (**3**–**5**) there are two sp^2 C–H groups and in all these cases both the sp^2 C–H are involved in C–H···N interactions. In addition, sp^3 C–H groups form C–H···π interactions that contribute to the molecular assembly within or between the sp^2 C–H···N networks. While the molecular constituents in **2** and **3**–**5** are similar in that both sp^2 and sp^3 C–H donors are present, the supramolecular situation in the latter is quite distinct in that sp^3 C–H groups also become effective. An increase in the number of sp^3 C–H donors may be the reason. The consistent involvement of sp^2 C–H in C–H···N and sp^3 C–H in C–H···π unveils an important feature of C–H group interactions. Within this weaker variety of interactions, the stronger donor (sp^2 C–H) contacts the stronger acceptor (N) and the weaker donor (sp^3 C–H) approaches the weaker acceptor (π system). Thus C–H group interactions exhibit a tendency unique to hydrogen bonds.[26]

In the trimethyl derivative **6**, sp^3 C–H donors are present in great excess over sp^2 C–H groups and the structure is practically governed by the C–H···N interactions of sp^3 C–H groups. In the tetramethyl derivative **7** only sp^3 C–H donors are present and they generate C–H···N networks. It is important to note that while the sp^3 C–H donors in **3**–**5** form C–H···π bonds, they are involved in C–H···N interactions in **6** and **7**. It appears that as long as stronger donors (sp^2 C–H) are available the weaker donors (sp^3 C–H) approach weaker acceptors (π system) while in the absence of stronger donors (or in the excess of weaker donors), the weaker donors interact with stronger acceptors (N).

The role of C–H···N interactions in crystal packing cannot be easily revealed in the presence of stronger interactions. As mentioned at the outset compounds **1**–**7** contain only C, H and N as constituent atoms and the competing effects are at a minimum. Consider the scatterplot of H···N distances *vs.* C–H···N angles (Fig. 8) for the C–H···N interactions in **1**–**7**. The decrease in H···N distances with increasing C–H acidity suggests the hydrogen bond character of C–H···N interactions. The fact that sp^2 C–H···N begin at shorter distances compared to those of sp^3 C–H···N suggests that the former type is stronger than the latter. Among the sp^3 C–H···N, the shortest are those from **6** and **7** wherein these interactions are operative structure fusing elements.

An analysis of the CSD for C–H···N contacts revealed that the sp^2-sp^3 C–H···N trend observed in compounds **1**–**7** is more general. The CSD (version 5.17, 197 481 entries)[27] has been searched for structures containing the elements C, H and N only, with at least one aromatic N atom. The search is restricted to those compounds that satisfy the conditions: $R \leqslant 0.10$, coordinate field present, no disorder and no charged residues. A database subset is created after manually excluding the structures with N–H and C≡N groups (to avoid strong donors and also acceptors with varying basicities) and duplicate hits with higher R value. A total of 726 C–H···N contacts (with H···N distances and C–H···N angles in the range 1.8 to 3.0 Å and 110 to 180°) are retrieved from this database subset. Fig. 9 is a histogram of C···N distances for sp^2 (shaded bars, 539 contacts) and sp^3 (dotted bars, 187 contacts) C–H···N interactions. The mean C···N distances for sp^2 and

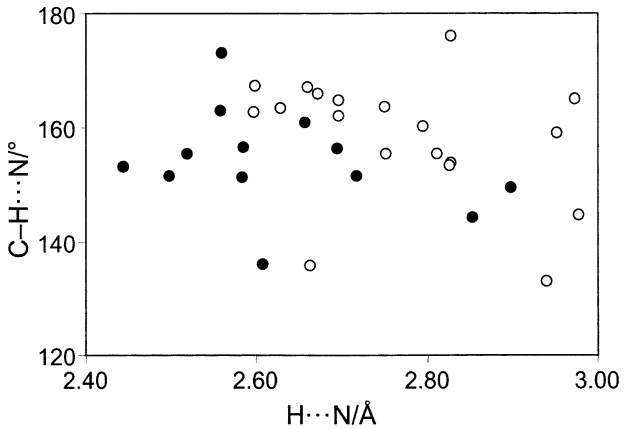


Fig. 8 Scatterplot of H···N distances *vs.* C–H···N angles in the structures **1**–**7**. Interactions of sp^2 and sp^3 C–H groups are shown as filled and open circles, respectively. Note that sp^2 C–H···N interactions begin at shorter distances compared to sp^3 C–H···N ones.

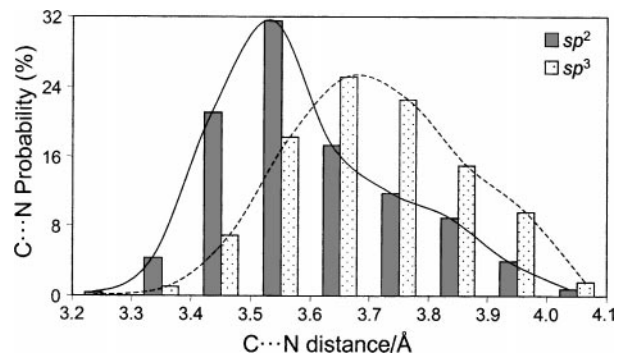


Fig. 9 Histogram of C···N distances for sp^2 (shaded) and sp^3 (dotted) C–H···N hydrogen bonds. The populations are expressed as percentages of observations. The bars at, say 3.45 Å, represent contacts between 3.4 and 3.5 Å. The probabilities are also expressed as distribution curves to accentuate the offset.

sp^3 contacts are 3.61 and 3.70 Å, respectively, and the probability histograms for these two are clearly offset according to the acidity of the C–H group. The more acidic the C–H group the shorter the C···N distance. Many of the shorter contacts in Fig. 9 arise from sp^2 C–H groups and both sp^2 and sp^3 C···N distances extend well beyond conventional van der Waals limit. These observations confirm that C–H···N interactions are not van der Waals contacts and that they resemble hydrogen bonds with their electrostatic character.[28]

Conclusion

The C–H···N interactions are the least studied variety of weak hydrogen bonds and in this work we adopted an experimental approach to understand the nature of these interactions. Compounds **1**–**7** have been chosen which consist of sp^2 and sp^3 C–H donors with N and π system acceptors. While C–H···N and C–H···π interactions are observed in the structures analysed, the former interaction is stronger than the latter. In the excess of any one type of C–H donor (*e.g.* sp^2 in **1**, **2** or sp^3 in **6**, **7**), C–H···N interactions are the sole structure determinants. When the two types of donors are in balance as in **3**–**5**, the stronger donors form C–H···N bonds while the weaker donors are involved in C–H···π interactions, suggesting the hydrogen bond-like character of C–H group interactions. For the C–H···N interactions in **1**–**7** the H···N distances decrease with increasing C–H acidity. This trend is observed for the first time in C–H···N interactions and they can be considered as weak hydrogen bonds. A similar trend is observed for C···N distances retrieved from the CSD. The similarity between sp^2 and sp^3 C–H···N networks in **4** and **7** indicates that any C–H group is similar in its structure steering character, irrespective of the C–H acidity. When the acidity is less the interaction is weaker and in many cases it is more likely supportive than operative. The sp C–H groups with greater acidity could form stronger C–H group interactions and efforts are currently underway to explore sp C–H···N hydrogen bonds in the deliberate design of crystal structures.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. V. R. T. thanks the Alexander von Humboldt Foundation for a postdoctoral fellowship.

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