

Even–odd effect in the co-crystals of pyrazine and dicarboxylic acids

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Abstract The co-crystals of pyrazine with dicarboxylic acids of the form $(\text{COOH})-(\text{CH}_2)_n-\text{COOH}$: oxalic ($n = 0$), malonic ($n = 1$) succinic ($n = 2$), glutaric ($n = 3$), adipic ($n = 4$), and pimelic ($n = 5$) acid, were synthesized and structurally characterized by means of X-ray diffraction. There are two principal structural motifs, depending on the stoichiometry: for 1:1 co-crystals, there are chains of alternate pyrazine and acid molecules, connected by strong $\text{O}-\text{H}\cdots\text{N}$ hydrogen bonds ($\cdots\text{pyr}\cdots\text{acid}\cdots\text{pyr}\cdots\text{acid}\cdots$) while for 2:1 stoichiometry the chains are made of pyrazine molecules and carboxylic acid centrosymmetric dimers ($\cdots\text{pyr}\cdots\text{acid}\cdots\text{acid}\cdots\text{pyr}\cdots$). The first possibility is observed for all acids in the series, while the second one only for these with odd numbers of methylene groups. The geometrical features of the acids do not show the clear indication for a reason of such behavior, the most probable reason can be connected with the possible symmetry of the acid molecule, C_i for n even, and with the mutual orientation of terminal carbonyl and hydroxyl groups, defined by improper $\text{O}=\text{C}\cdots\text{C}=\text{O}$ torsion angles, which are close to 180° for even and have much smaller values for odd n values.

Keywords Co-crystals · Crystal engineering · Hydrogen bonds · Pyrazine · Dicarboxylic acids

Introduction

The self-organization of molecules in order to form well-defined supramolecular structures under the influence of weak forces such as hydrogen bonds and van der Waals interaction is still being explored extensively. The parallels between such *supramolecular synthesis* and chemical, *molecular synthesis* were stressed by a number of authors (e.g. [1–4]). What's more, structural crystallography can be regarded as one of primary tools in studying such processes (for instance [5, 6]) as—using the term coined by Dunitz [7]—the molecular crystal itself is “*the supermolecule par excellence*: a lump of matter, of macroscopic dimensions, millions of molecules long, held together in a periodic arrangement by just the same kind of interactions as are responsible for molecular recognition and complexation at all levels.”

Preparation of the co-crystals in fact is the supramolecular synthesis: using the weak interactions to obtain new materials with properties different from those of the component molecules. It might be worth mentioning that the very term “co-crystals” has been fiercely debated (e.g. [8, 9]), for instance, Desiraju [8] regarded the term ‘molecular complex’ as more appropriate. The questions about the solvates on one hand and salts on the other were also raised, and—as in many cases regarding the terminology, classification etc.—this ambiguity may well stay unresolved.

For the reasons of this paper, we will use the term “co-crystal” in its widely accepted sense (e.g. as used by Stahly [10]): as the solid which consists of two or more components that form a unique crystalline structure having unique properties.

The even–odd alternation of the solid-state physical properties within the series of n -alkane derivatives is known for almost 150 years; it was first observed for the

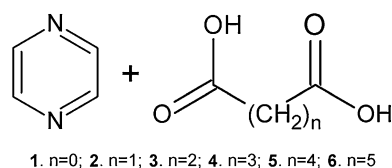
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melting points of α,ω -alkanedicarboxylic acids [11] — those with even number of methylene groups have systematically higher melting points compared to the odd ones, and further for other derivatives and other properties (solubility, thermal expansion [12], elastic moduli [13]. Thalladi et al. [14] compared the crystal structures of the series of diacids of the formula $\text{HOOC}-(\text{CH}_2)_n-\text{COOH}$ ($n = 0 \div 8$) and concluded that the principal structural motifs are similar in both series (hydrogen-bonded dimers, stacks of methylene chains), while the differences include the conformation of the chains (in general, all-trans for even, twisted for odd), and the offset along the chain within the stack. They also confirmed the general rule stated by Dupré la Tour in 1930's [15] that dimorphism is common between the odd acids and is rarely observed for even ones.

Gopalan et al. [16] determined the experimental charge density in the crystals of aliphatic dicarboxylic acids (from malonic to pimelic) on the basis of high-resolution X-ray diffraction. They also found the even–odd alternation of certain molecular and crystal characteristics: dipole moments, as calculated from the pseudoatomic charges are systematically larger for odd acids, while the reverse trend was observed for the charges of atoms involved in side-chains interactions.

Our observations during the studies of the salts of acetic acid and its halogeno-derivatives and α,ω -diaminoalkanes [17, 18] showed that the crystallization of the ‘odd’ salts is much more difficult than for the ‘even’ analogs, and it is reflected in the number of appropriate hits in the Cambridge Structural Database [19]. We have performed a similar survey for the α,ω -alkanedicarboxylic acids (CSD version 5.34, last update May 2013, duplicate hits excluded) show that the same alternation is found for this group of compounds (Fig. 1).

In this work, we present the crystallographic structures of hydrogen-bonded adducts obtained by the co-crystallization of pyrazine with dicarboxylic acids of the form $(\text{COOH})-(\text{CH}_2)_n-\text{COOH}$ (Scheme 1): oxalic ($n = 0$),



Scheme 1 The studied co-crystals

malonic ($n = 1$) succinic ($n = 2$), glutaric ($n = 3$), adipic ($n = 4$), and pimelic ($n = 5$).

Pyrazine as a difunctional basis seems to make an interesting component for supramolecular synthesis, and it actually has been used for this reason quite often, for instance with different tartaric acids [20], hydrobenzoic acids [21], or n -alkyl-carboxylic acids [22, 23]. It might be noted that one of the very first examples of halogen bonding—although not named as such yet—were found in 1960's in the isomorphous co-crystals of pyrazine and tetrabromo- and tetraiodoethylene [24]. On the other hand, some dicarboxylic acids were also used for co-crystallization (e.g. [25–29]). It seemed also interesting to recognize if the even–odd effect will be visible in this series of compounds.

Recently, the crystal structure of the mechanically prepared co-crystal of pyrazine with succinic acid has been published [30]. Although this structure is identical with the one referred in our paper, we decided to include here the structure determined by us, as the crystals reported here were obtained by slow crystallization.

Our goal was to determine the influence of the environment of carboxylic groups (in particular, aliphatic chain length) on the formation and resulting structures of the co-crystals with pyrazine. In principle, at least two different modes of building the mixed supramolecular synthons (or heterosynthons) seemed to be available: in one we could expect the alternate ...pyrazine...acid...pyrazine...acid chains, in the other we can also have the acid...acid hydrogen-bonded dimer (...pyrazine...acid...acid...pyrazine...). Of course, one can imagine more possibilities: catameric bonds between the acids (not dimers), more complicated acid structures etc.

Experimental

General procedure

All chemicals were purchased from Aldrich and were used as received without further purification. Complexes of pyrazine and carboxylic acids were prepared in a single solution or in solvent mixture. Solutions were left uncovered and allowed to evaporate slowly at room temperature

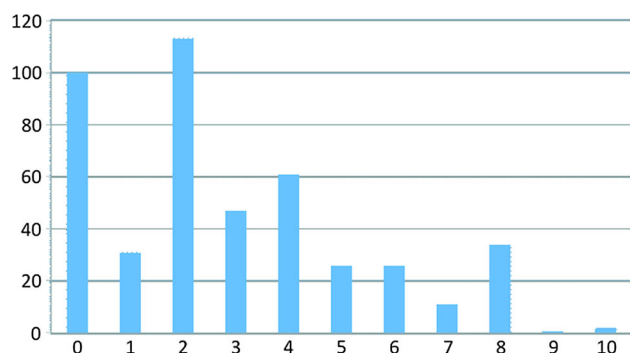


Fig. 1 Numbers of structures of α,ω -alkanedicarboxylic acids in the CSD as a function of a number of carbon atoms in the aliphatic chain

until crystals appeared, the crystallization process took from minutes to weeks. For example, in case of oxalic acid, the crystals appeared almost instantly after cooling the reaction mixture.

Co-crystals preparation

(1) 65 mg (0.81mmol) of pyrazine and 70 mg (0.78 mmol) of oxalic acid were dissolved in 2 mL of ethanol and heated.

(2) 150 mg (1.87 mmol) of pyrazine and 70 mg (0.67mmol) of malonic acid were dissolved in 2 mL of acetone and heated.

(2a) 50 mg (0.63mmol) of pyrazine and 65 mg (0.63mmol) of malonic acid were dissolved in 2 mL of water and heated.

(3) 50 mg (0.63mmol) of pyrazine and 65 mg (0.55 mmol) of succinic acid were dissolved in 2 mL of water and heated.

(4) 130 mg (1.62mmol) of pyrazine and 110 mg (0.81mmol) of glutaric acid were dissolved in 2 mL of acetone and heated.

(4a) 65 mg (0.81mmol) of pyrazine and 110 mg (0.81mmol) of glutaric acid were dissolved in 2 mL of acetone and heated.

(5) 50 mg (0.63mmol) of pyrazine and 90 mg (0.62mmol) of adipic acid were dissolved in 2 mL of acetone and heated.

(6) 120 mg (1.5mmol) of pyrazine and 120 mg (0.75mmol) of pimelic acid were dissolved in 2 mL of acetone and heated.

(6a) 50 mg (0.63mmol) of pyrazine and 100 mg (0.63mmol) of pimelic acid were dissolved in 2 mL of acetone and heated.

In the cases, when only one of the co-crystal stoichiometry was obtained (1, 3, and 5) a numerous tries with the large excess of the acid were performed but in every case no different crystals were formed.

In general, crystals appeared from seconds (1) to days after preparing the solution. No estimation of yield was performed as—for instance—sometimes the crystals of components could be also found in the crystalline products.

X-ray diffraction

Diffraction data were collected on an Agilent Technologies Xcalibur diffractometer with an EOS CCD area detector (fine-focus tube, MoK α , $\lambda = 0.71073 \text{ \AA}$) for 2, 2a, 5, 6, 6a at 100(1) K, and on Agilent Technologies SuperNova diffractometer with an Atlas CCD area detector (microfocus tube, CuK α , $\lambda = 1.54178 \text{ \AA}$) for 1, 4, and 4a at 130(1) K, and for 3 at 295(1) K. The data collections for the crystals

were performed with CrysAlis^{Pro} [31]. Unit cell parameters were determined by the least-squares procedure for the reflections chosen from the whole datasets on the basis of their intensities. The data were corrected for Lorentz and polarization effects, as well as for absorption, by empirical correction using spherical harmonics, implemented in the SCALE3 ABSPACK scaling algorithm. All structures were determined by direct methods using SIR92 [32] and refined by the full-matrix least-squares method with SHELXL-97 [33] (these procedures were performed within WinGX suite of programs [34]). The crystals of 2 turned out to be twins, it was taken into account in the data reduction [31] and in refinement [33]. The BASF parameter, the ratio of two components, refined at 0.144(8).

All non-hydrogen atoms were refined with anisotropic displacement parameters. In 2 and 6, hydrogen atoms from C–H groups were generated geometrically and refined as ‘riding’ on their parent atoms; their isotropic displacement parameters were set at 1.2 times U_{eq} of their parent atoms. The O–H hydrogen atoms in these two structures and all hydrogen atoms in the remaining structures were located from difference electron density maps and isotropically refined. Table 1 lists the relevant crystallographic data together with the refinement details.

Results and discussion

Oxalic acid : pyrazine 1:1 (1)

This structure crystallizes in the non-centrosymmetric Cc space group (the only one such a case in the whole studied series!), therefore the supramolecular structures which are observed here can not have the internal symmetry.

The acid molecule is almost planar, the dihedral angles between the carboxylic groups (which are in trans arrangement, HO–C–C–OH torsion angle is 173.4(2)°). The principal supramolecular motif in 1 is the flat chain created by alternate acid and pyrazine molecules connected by short, almost linear hydrogen bonds (Fig. 1; Table 2 lists the hydrogen bond data for all the compounds). Weak intra-chain C–H \cdots O hydrogen bonds within the chain are rather artefacts of the primary, strong interactions. Hereinafter, we will discuss the C–H \cdots O hydrogen bonds on the basis of both geometrical features and of their role on the crystal structure, either structure-directing or just mere secondary [35–39]. In the case of 1, the above-mentioned interactions are rather of secondary nature, but the inter-chain C–H \cdots O bonds (vide infra) are definitively playing important role in the building of crystal structure.

Further organization of the chains is determined by the relatively strong and linear (Table 2) inter-chain C–H \cdots O hydrogen bonds (Fig. 2), which create the flat layers of

Table 1 Crystal data, data collection and structure refinement

Compound	1	2	2a	3	4
Formula	C ₂ H ₂ O ₄ · C ₄ H ₄ N ₂	C ₃ H ₄ O ₄ · C ₄ H ₄ N ₂	2(C ₃ H ₄ O ₄)· (C ₄ H ₄ N ₂)	C ₄ H ₆ O ₄ · C ₄ H ₄ N ₂	C ₅ H ₈ O ₄ · C ₄ H ₄ N ₂
Formula weight	170.13/c	184.15	288.22	198.18	212.21
Crystal system	monoclinic	triclinic	triclinic	monoclinic	Monoclinic
Space group	Cc	P-1	P-1	P2 ₁ /n	P2 ₁ /c
a (Å)	10.7607 (5)	5.6075 (10)	5.0304 (8)	8.5282 (4)	11.5578 (3)
b (Å)	10.7828 (3)	7.7936 (14)	5.1220 (7)	5.1299 (2)	10.7119 (2)
c (Å)	6.8283 (3)	10.1208 (18)	12.1315 (10)	10.3033 (4)	8.6781 (2)
α (°)	90	107.141 (16)	81.20 (2)	90	90
β (°)	117.378 (6)	103.099 (15)	83.10 (2)	102.916 (4)	110.185 (3)
γ (°)	90	95.354 (14)	78.976 (13)	90	90
V (Å ³)	703.55 (6)	405.53 (14)	304.54 (7)	439.35 (3)	1008.41 (4)
Z	4	2	1	2	4
D _x (g cm ⁻³)	1.61	1.51	1.57	1.50	1.40
F(000)	352	192	150	208	448
μ (mm ⁻¹)	1.20	0.13	0.14	1.04	0.94
Reflections:					
collected	2386	2736	1952	1491	4033
unique (R _{int})	1100 (0.013)	1414 (0.035)	1242 (0.013)	854 (0.009)	1993 (0.017)
with I > 2σ(I)	1096	1114	1021	825	1833
R(F) [I > 2σ(I)]	0.024	0.072	0.033	0.032	0.033
wR(F ²) [I > 2σ(I)]	0.068	0.177	0.083	0.087	0.088
R(F) [all data]	0.024	0.088	0.041	0.033	0.035
wR(F ²) [all data]	0.068	0.194	0.087	0.088	0.090
Goodness of fit	1.09	1.11	1.02	1.08	1.04
max/min Δρ (e·Å ⁻³)	0.29/-0.19	0.33/-0.33	0.20/-0.24	0.30/-0.22	0.26/-0.14
Compound	4a	5	6	6a	
Formula	2(C ₅ H ₈ O ₄)·C ₄ H ₄ N ₂	C ₆ H ₁₀ O ₄ ·C ₄ H ₄ N ₂	C ₇ H ₁₂ O ₄ ·C ₄ H ₄ N ₂	2(C ₇ H ₁₂ O ₄)·(C ₄ H ₄ N ₂)	
Formula weight	344.32/c	226.23	240.26	400.42	
Crystal system	monoclinic	triclinic	monoclinic	triclinic	
Space group	P2 ₁ /n	P-1	P2 ₁ /c	P-1	
a (Å)	8.7000 (3)	5.3622 (19)	7.4741 (9)	5.1426 (11)	
b (Å)	5.4035 (2)	6.939 (2)	6.9544 (11)	7.1389 (14)	
c (Å)	17.1900 (7)	7.607 (4)	22.846 (4)	14.2675 (14)	
α (°)	90	96.95 (3)	90	98.278 (12)	
β (°)	95.723 (3)	94.74 (4)	95.390 (14)	93.208 (12)	
γ (°)	90	104.91 (3)	90	103.277 (18)	
V (Å ³)	804.08 (5)	269.61 (18)	1182.2 (3)	502.32 (15)	
Z	2	1	4	1	
D _x (g cm ⁻³)	1.42	1.39	1.35	1.32	
F(000)	364	120	512	214	
μ (mm ⁻¹)	1.01	0.11	0.10	0.10	
Reflections					
collected	5520	1891	3923	3447	
unique (R _{int})	1595 (0.015)	1117 (0.018)	2072 (0.053)	2035 (0.022)	
with I > 2σ(I)	1565	911	1143	1645	
R(F) [I > 2σ(I)]	0.029	0.041	0.073	0.040	
wR(F ²) [I > 2σ(I)]	0.072	0.087	0.103	0.090	

Table 1 continued

Compound	4a	5	6	6a
R(F) [all data]	0.029	0.053	0.142	0.053
wR(F ²) [all data]	0.073	0.094	0.125	0.098
Goodness of fit	1.08	1.03	0.99	1.06
max/min $\Delta\rho$ (e \cdot Å ⁻³)	0.24/−0.18	0.19/−0.26	0.30/−0.29	0.19/−0.24

A note regarding numbering scheme. Because the details in the figures might be too small, here are the principal rules we have chosen for the numbering of atoms. In general, acid atoms have letter A after the number and those from pyrazine – B. If there is more than one symmetry-independent pyrazine, the second one gets a letter C. In the acid, numbering is consecutive along the carbon chain and the oxygen atoms have the numbers related to the carbon atom to which they are bonded. The oxygen atom with the last digit ‘1’ (e.g. O11A) is always a hydroxyl, while this with ‘2’ (O12A) – carbonyl

molecules, approximately perpendicular to the b-direction. These layers, in turn, interact by means of $\pi\cdots\pi$ stacking interactions with one another. The dihedral angle between the ring planes—related by c-glide—in stack is as small as 3.4°, the inter-planar distance is 3.22Å with almost 35 % overlap between the aromatic pyrazine rings.

Using the graph-set notation [38, 39], the motifs of the structure can be described by C(10) < R₂²(7) > chains with second-rank intra-chain rings, while inter-chain weaker interactions would add R₂²(4), R₂²(8), and R₄⁴(10) rings, cf. Fig. 2. In general, simple chain motifs of increasing length (with increasing number of carbon atoms) are observed in all the crystals with 1:1 stoichiometry.

It might be noted that despite using different ratios of the reagents and various crystallization conditions, in this case we were not able to get any other form of the molecular complex.

Malonic acid : pyrazine 1:1 (**2**) and 2:1 (**2a**)

For this combination (one methylene group between the carboxylic functions in the diacid molecule), we were able to prepare two different crystals, with different stoichiometry.

The complex **2**—obtained with the great, almost 3:1, excess of pyrazine—crystallizes in the P-1 triclinic space group, and the asymmetric unit contains one acid molecule and two independent halves of pyrazine moieties lying across two different inversion centers at 0,1/2,0 and 0,1/2,1/2. In the crystal structure, the chains of hydrogen-bonded acid and pyrazine molecules, in the sequence ...pyrazine1...acid...pyrazine2...acid...pyrazine1..., are the main motif (Fig. 3a). In principle, the main graph-set motif should be described as a C₄⁴(22) chain.

Even though the symmetry-independent pyrazine rings in the chain are almost parallel—dihedral angle between their planes is only 5.2(9)°—they are not coplanar, actually the chain is more stairs-like or zigzag (Fig 3b). This conformation of the chain is achieved by the large twist between the carboxylic groups in the acid molecule

(dihedral angle is 82.4(4)°). For this reason, there are no intra-chain secondary C–H...O interactions in **2**. The inter-chain C–H...O hydrogen bonds, however, longer and presumably weaker than in **1**, organize the chains into centrosymmetric pairs, and further into 3D structure.

In the asymmetric unit of co-crystal **2a**, there are one acid molecule and a half of pyrazine which lies across the center of inversion at 1/2,0,0; so the stoichiometry of this complex is 2:1 (acid:pyrazine). Interestingly, this composition was obtained even though the molar ratio of the components was 1:1. There are hydrogen-bonded chains in this structure, but the acid molecules within these chains make one homomolecular centrosymmetric R₂²(8) dimer, so the sequence of molecules in the chain is as follows: pyrazine...acid...acid...pyrazine...acid...acid...pyrazine (Fig. 4a). The main motif is therefore C₃³(18) < R₂²(8) >. Intra-chain C–H...O hydrogen bonds are obviously of secondary nature. The two different kinds of centers of inversion are located in the middle of pyrazine rings and between the acid molecules connected by hydrogen bonds.

Also, in this case, the carboxylic groups are almost perpendicular to each other (dihedral angle 88.30(12)°) and the chain is stairs-like, with exactly parallel pyridine rings (Fig. 4b); weak, but at least to some extent pattern-determining, inter-chain C–H...O interactions can be found, which create R₄⁴(14) and R₆⁶(32) rings, and chains of acid molecules with two different R₂²(8) hydrogen-bonded rings (Fig. 4c)

Succinic acid: pyrazine 1:1 (**3**)

Succinic acid co-crystallizes with pyrazine in 1:1 ratio and despite numerous tries we were not able to get another stoichiometry. The asymmetric part of the unit cell contains half of pyrazine (across inversion center at 1/2,0,0) and half of the succinic acid molecule (inversion center at 0,0,0). The main structural motif is the hydrogen-bonded ribbon—approximately parallel to (210) plane—of alternating pyrazine and acid molecules (Fig. 5).

Table 2 Hydrogen-bond data (Å, °)

D	H	A	D-H	H...A	D...A	D-H...A
1						
O11A	H11A	N1B	0.95 (4)	1.70 (4)	2.6435 (19)	171 (4)
O21A	H21A	N4B ⁱ	0.93 (3)	1.70 (3)	2.6226 (19)	177 (3)
C2B	H2B	O12A	0.92 (3)	2.65 (3)	3.293 (2)	128 (2)
C5B	H5B	O22A ⁱⁱ	0.96 (3)	2.59 (3)	3.2774 (19)	129 (2)
C3B	H3B	O11A ⁱⁱⁱ	0.99 (3)	2.41 (3)	3.369 (2)	165.2 (19)
C6B	H6B	O21A ⁱⁱⁱ	0.93 (2)	2.48 (2)	3.379 (2)	162 (2)
2						
O11A	H11A	N1C	0.91 (5)	1.83 (5)	2.730 (4)	170 (4)
O31A	H31A	N1C	0.91 (7)	1.75 (7)	2.659 (4)	171 (6)
C3B	H3B	O12A ^{iv}	0.93	2.57	3.399 (4)	149
C2C	H2C	O12A ^v	0.93	2.47	3.229 (4)	139
2a						
O11A	H11A	N1B	0.99 (2)	1.70 (2)	2.6886 (15)	172.8 (19)
C2B	H2B	O12A	0.957 (15)	2.604 (15)	3.2759 (17)	127.5 (12)
O31A	H31A	O32A ^{vi}	0.97 (2)	1.69 (2)	2.6573 (14)	177.5 (18)
C2B	H2B	O12A ^{vii}	0.957 (15)	2.482 (16)	3.2022 (17)	132.0 (12)
C2A	H2A2	O32A ^{viii}	0.925 (16)	2.552 (16)	3.3097 (18)	139.4 (12)
3						
O11A	H11A	N1B	0.92 (2)	1.81 (2)	2.7257 (12)	177.8 (18)
C2B	H2B	O12A ^{ix}	0.950 (15)	2.542 (14)	3.1676 (14)	123.6 (11)
C2B	H2B	O11A ^x	0.950 (15)	2.555 (15)	3.4075 (13)	149.5 (11)
C3B	H3B	O12A ^{xi}	0.961 (17)	2.656 (16)	3.3417 (13)	128.7 (12)
4						
O11A	H11A	N4B	0.93 (2)	1.83 (2)	2.7231 (12)	158.9 (18)
O51A	H51A	N1B ^{xii}	0.932 (19)	1.813 (19)	2.7440 (12)	176.4 (17)
C5B	H5B	O12A ^{xiii}	0.969 (15)	2.382 (15)	3.3484 (14)	174.6 (12)
C6B	H6B	O52A ^{xiii}	0.959 (14)	2.371 (14)	3.2793 (14)	158.0 (11)
C2B	H2B	O52A ^{xiv}	0.975 (15)	2.416 (14)	3.1577 (14)	132.4 (11)
4a						
O11A	H11A	N1B	0.929 (18)	1.806 (18)	2.7330 (12)	175.1 (15)
O51A	H51A	O52A ^{xv}	0.90 (2)	1.75 (2)	2.6484 (11)	174.8 (19)
C2B	H2B	O51A ^{xvi}	0.974 (14)	2.465 (14)	3.3305 (13)	147.9 (12)
C3B	H3B	O12A ^{xvii}	0.986 (15)	2.499 (14)	3.2209 (13)	129.8 (10)
5						
O11A	H11A	N1B	0.95 (2)	1.78 (2)	2.723 (2)	177 (2)
C2B	H2B	O12A ^{xviii}	0.982 (16)	2.316 (16)	3.230 (2)	154.5 (12)
C3B	H3B	O12A ^{xix}	0.996 (15)	2.587 (16)	3.313 (2)	129.7 (12)
6						
O11A	H11A	N1B ^{xx}	0.97 (4)	1.73 (4)	2.684 (4)	167 (4)
O71A	H71A	N1C ^{xxi}	0.87 (3)	1.87 (3)	2.733 (4)	174 (3)
C2B	H2B	O11A ^{xxii}	0.93	2.32	3.242 (5)	174
C2C	H2C	O72A	0.93	2.57	3.258 (5)	132
6a						
O11A	H11A	N1B	0.92 (2)	1.79 (2)	2.7160 (16)	176 (2)
O71A	H71A	O72A ^{xxiii}	0.93 (2)	1.75 (2)	2.6773 (16)	175.9 (19)
C2B	H2B	O12A ^{xxiv}	0.950 (17)	2.363 (17)	3.223 (2)	150.4 (13)

^a Symmetry codes: ⁱ $x, 1 + y, z$; ⁱⁱ $x, -1 + y, z$; ⁱⁱⁱ $-1/2 + x, -1/2 + y, z$; ^{iv} $1/2 + x, -1/2 + y, z$; ^v $-x, -y, 2 - z$; ^{vi} $-1 + x, y, z$; ^{vii} $2 - x, -y, 1 - z$; ^{viii} $2 - x, 1 - y, -z$; ^{ix} $1 - x, 1 - y, 1 - z$; ^x $1/2 + x, 1/2 - y, 1/2 + z$; ^{xi} $1/2 - x, -1/2 + y, 1/2 - z$; ^{xii} $1 - x, -y, -z$; ^{xiii} $3/2 + x, 1/2 - y, 1 + z$; ^{xiiii} $1 - x, -y, 1 - z$; ^{xv} $-3/2 + x, 1/2 - y, -1 + z$; ^{xvi} $-x, 1 - y, 1 - z$; ^{xvii} $1/2 + x, -3/2 + y, 3/2 + z$; ^{xviii} $-x, -1 - y, 2 - z$; ^{xix} $x, 1 + y, z$; ^{xx} $3 - x, 2 - y, 2 - z$; ^{xxi} $1 + x, y, -1 + z$; ^{xxii} $-1 + x, y, z$; ^{xxiii} $1 - x, 1 - y, 1 - z$; ^{xxiv} $1 - x, 3 - y, 1 - z$; ^{xxv} $x, -1 + y, z$

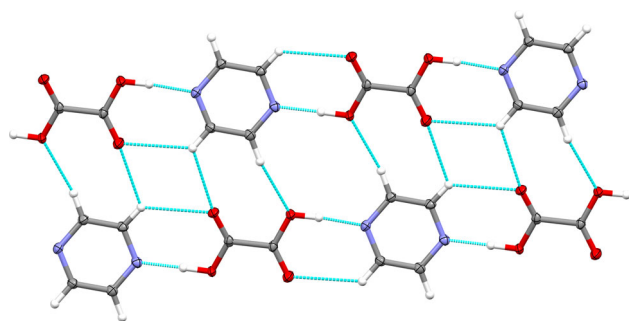


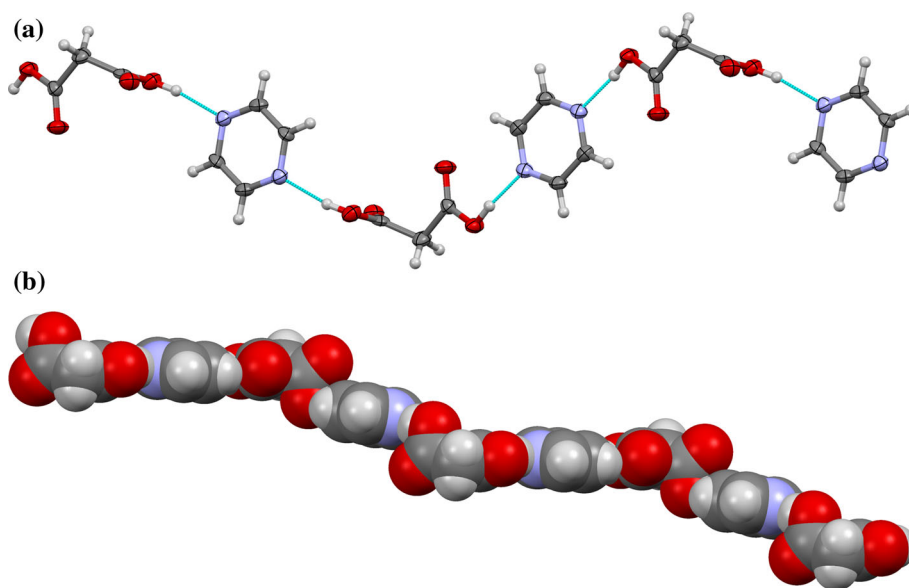
Fig. 2 Hydrogen-bonded layer of alternating pyrazine and oxalic acid molecules in **1**. Ellipsoids are drawn at the 50 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii; hydrogen bonds are shown as *dashed blue lines*

Due to symmetry (C_i), both fragments are planar, the acid molecule is in fully extended conformation (C–C–C–C torsion angle 180° , cf. Table 3), and the ribbons are also flat. In the crystal structure (monoclinic space group $P2_1/n$), there are almost perpendicular ribbons, connected by means of weak C–H \cdots O interactions (Table 2), which create infinite chains and—as always—by van der Waals forces (Fig. 6).

Glutaric acid : pyrazine 1:1 (**4**) and 2:1 (**4a**)

For glutaric acid, we have found that two different structures, of different stoichiometry, are formed. In the first one, the acid to pyrazine ratio is 1:1, both molecules are in general positions and in the crystal structure and there are chains of alternate pyrazine and glutaric acid (in an extended *trans–trans* conformation, Table 3) molecules, connected by strong O–H \cdots N hydrogen bonds and by secondary—but relatively short—C–H \cdots O hydrogen bonds

Fig. 3 a A fragment of hydrogen-bonded chain of pyrazine and malonic acid molecules. The ellipsoids are drawn at the 70 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds. **b** the same chain as seen side-on



(Fig. 7). However, it can be seen that—probably due to the demands of further crystal architecture—this secondary weak hydrogen bond is observed only on one side of the (unsymmetrical) acid molecule.

The neighboring ribbons—one can note that they are significantly twisted—are connected by relatively very short and directional C–H \cdots O bonds (cf. Table 2) to form the layer of molecules, approximately parallel to (10–1) plane. Fig. 8 shows such a plane—it is evident that the formation and stability of this plane is possible because the C–H donors from one side of the pyrazine molecule and C=O acceptors from one acid fit perfectly, one set to another. As can be seen in Fig. 8, the structure-determining motifs, created by these bonds are rings $R_2^2(11)$, $R_4^4(14)$ and a larger one, $R_6^6(34)$. These layers are further only very weakly bound to give the three-dimensional crystal structure.

The second co-crystal of pyrazine and glutaric acid is structurally similar to 2:1 co-crystal of pyrazine and malonic acid (**2a**). The asymmetric part of the unit cell contains one acid molecule (in different *trans–gauche* conformation, Table 3) and half of the C_i -symmetric pyrazine molecule (so the stoichiometry of this compound is 2:1), and in the crystal structure, there are chains of hydrogen-bonded molecules in the sequence: ...pyrazine \cdots acid \cdots acid \cdots pyrazine \cdots acid \cdots acid..., and the subsequent centers of inversion are at middle points of pyrazine rings and of hydrogen-bonded $R_2^2(8)$ rings in the carboxylic acid dimers (Fig. 9).

The weak inter-chain C–H \cdots O hydrogen bonds connect mutually nearly perpendicular chains, giving packing diagrams similar to that observed for **3** (Fig. 6). The dihedral angle between the COO groups is also large in this case, equal $74.75(10)^\circ$ —in contrast, in **4** the acid molecule is

Fig. 4 a A fragment of hydrogen-bonded chain of pyrazine and malonic acid molecules. The ellipsoids are drawn at the 70 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds. **b** the same chain as seen side-on, **c** the chain of acid molecules

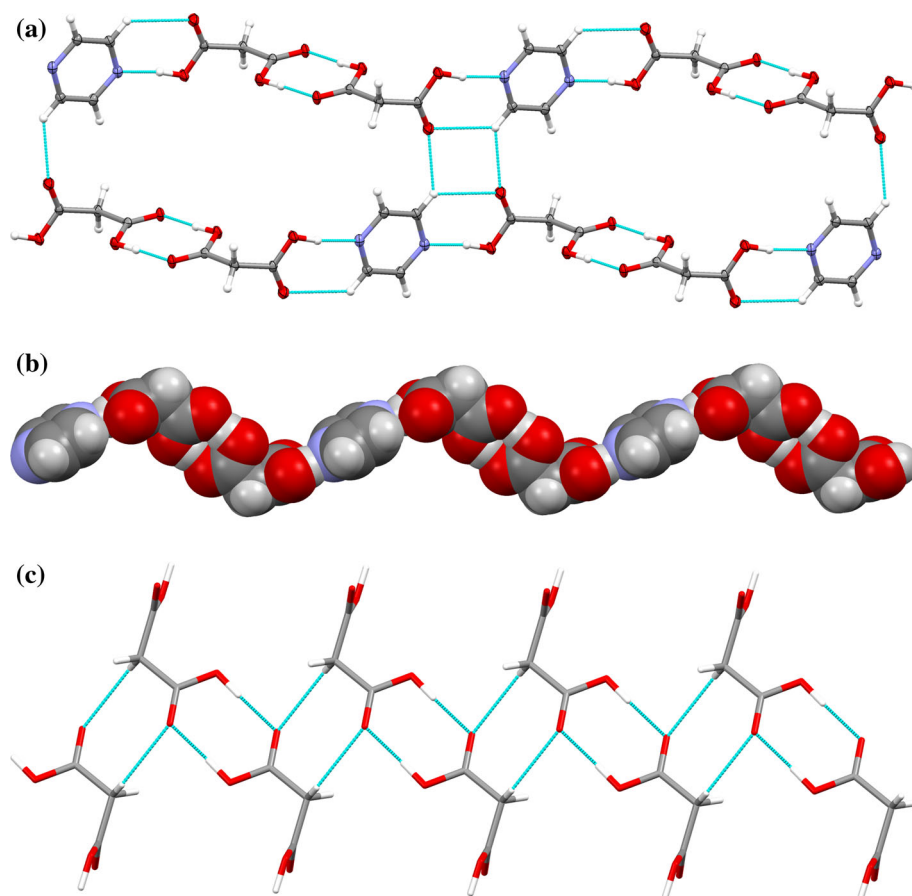


Fig. 5 Hydrogen-bonded flat chain of pyridine and succinic acid molecules. Ellipsoids are drawn at the 50 % probability level, hydrogen atoms are shown as *spheres* of arbitrary radii, hydrogen bonds—as *dashed blue lines*

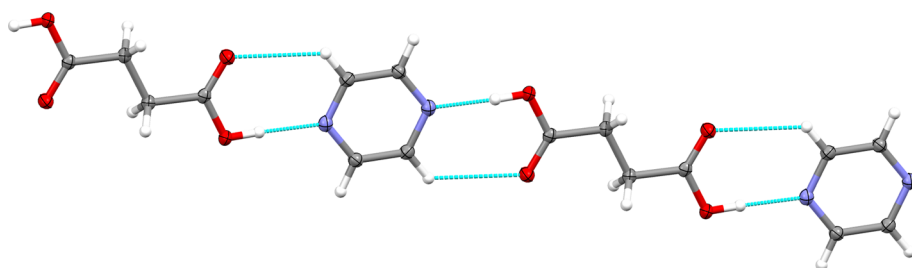


Table 3 Some selected geometrical parameters (°): dihedral angle between the planes of carboxylic groups, torsion angles along the carbon chains and the improper torsion angles between the carbonyl groups; *n* is a number of C atoms in the aliphatic chain

	1	2	2a	3	4	4a	5	6	6a
N	0	1	1	2	3	3	4	5	5
COO/COO	8.0 (2)	82.4 (4)	88.3 (1)	0	8.5 (2)	74.8 (2)	0	47.7 (3)	50.0 (2)
C–C–C–C				180	179.9 (1)	–177.4 (1)	173.9 (2)	174.4 (3)	173.5 (1)
					176.2 (1)		180	179.2 (3)	169.5 (1)
						74.2 (1)	–173.9 (2)	173.9 (3)	173.0 (1)
								–175.8 (3)	171.2 (1)
O=C⋯C=O	170.8	63.8	72.8	180	8.3	–88.1	180	28.1	49.3

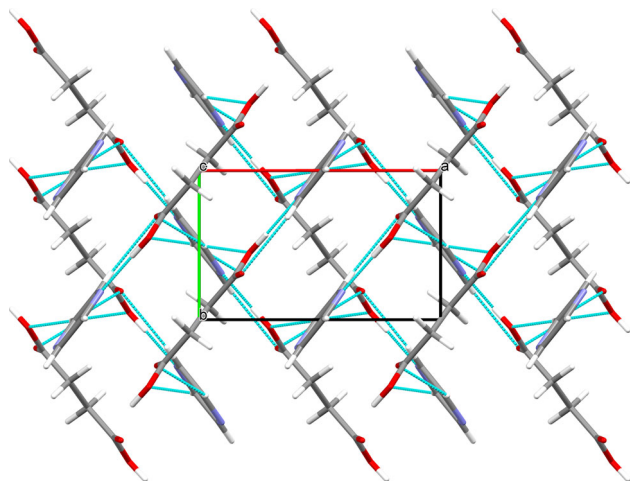


Fig. 6 Crystal packing of **3** as seen along *z*-direction; hydrogen bonds and weaker interactions are shown as *dashed blue lines*

almost planar, the dihedral angle between carboxylic groups is $8.5(2)^\circ$.

Adipic acid : pyrazine 1:1 (**5**)

For this combination, we were again able to obtain only one co-crystal, of stoichiometry 1:1. Asymmetric unit contains halves of both components (C_i symmetrical: acid lies across the center of inversion at $1/2, 0, 1/2$, while

Fig. 7 Hydrogen-bonded chain of pyridine and glutaric acid molecules. Ellipsoids are drawn at the 50 % probability level, hydrogen atoms are shown as *spheres* of arbitrary radii, hydrogen bonds—as *dashed lines*

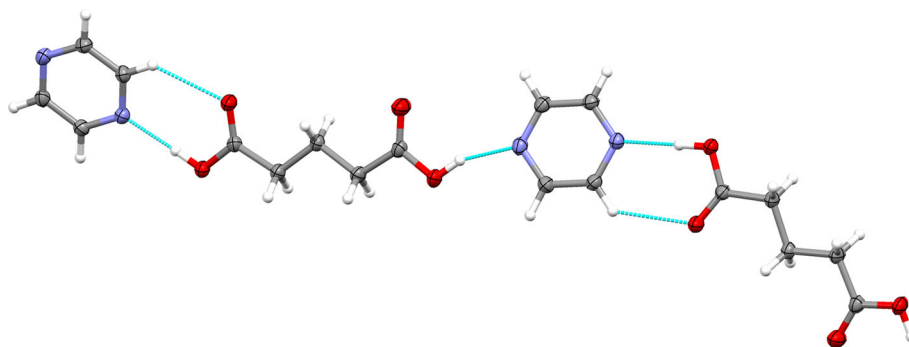
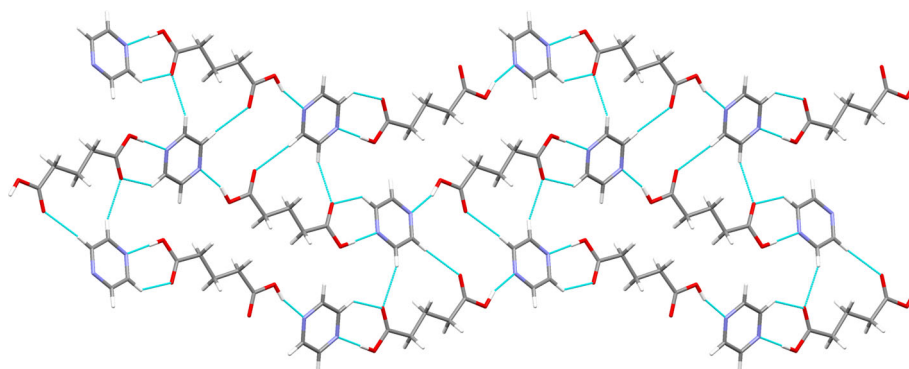


Fig. 8 The layer of the molecules in the crystal structure **4** as seen approximately along *z*-direction



pyrazine—at $1/2, 0, 0$, in the triclinic space group $P-1$). The acid molecule adopts symmetrical all-*trans* conformation. Similar disposition of elements was observed in the complex with succinic acid (**3**). In fact, the basic motifs of crystal packing are very similar: alternate acid and pyrazine molecules, lying on the subsequent centers of inversion, and connected by hydrogen bonds (Fig. 10).

Neighboring chains are connected by very short C–H...O hydrogen bonds and make the layer of molecules rings $R_4^2(10)$ and $R_4^4(24)$; and these layers interact only very weakly (C–H...O contacts longer than 2.7\AA , no π – π stacking) with one another.

Pimelic acid : pyrazine 1:1 (**6**) and 2:1 (**6a**)

For pimelic acid, in turn, we have observed two different co-crystals with the stoichiometries 1:1 and 2:1.

In the 1:1 co-crystal, the disposition of components is similar to that found in **2**: the asymmetric part of the unit cell contains one acid molecule (all-*trans* conformation, Table 3) and two independent halves of pyrazines, across the different inversion centers at $0, 0, 1/2$ and $1/2, 0, 0$; these molecules are connected by hydrogen bonds into the chain with sequence identical to that found in **2**: ...pyrazine1...acid...pyrazine2...acid...pyrazine1... Interestingly, orientation of the molecules in these chains does not allow for secondary C–H...O hydrogen bonds. The asymmetry

Fig. 9 A fragment of hydrogen-bonded chain of pyrazine and glutaric acid molecules. The ellipsoids are drawn at the 50 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds

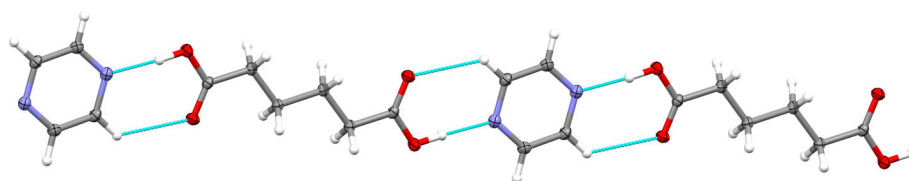
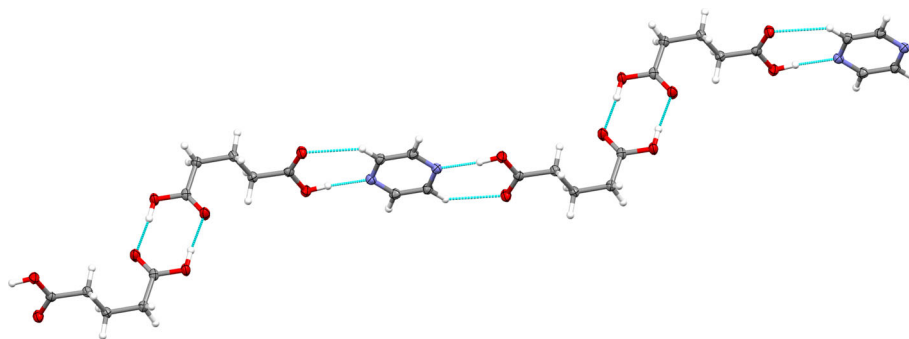
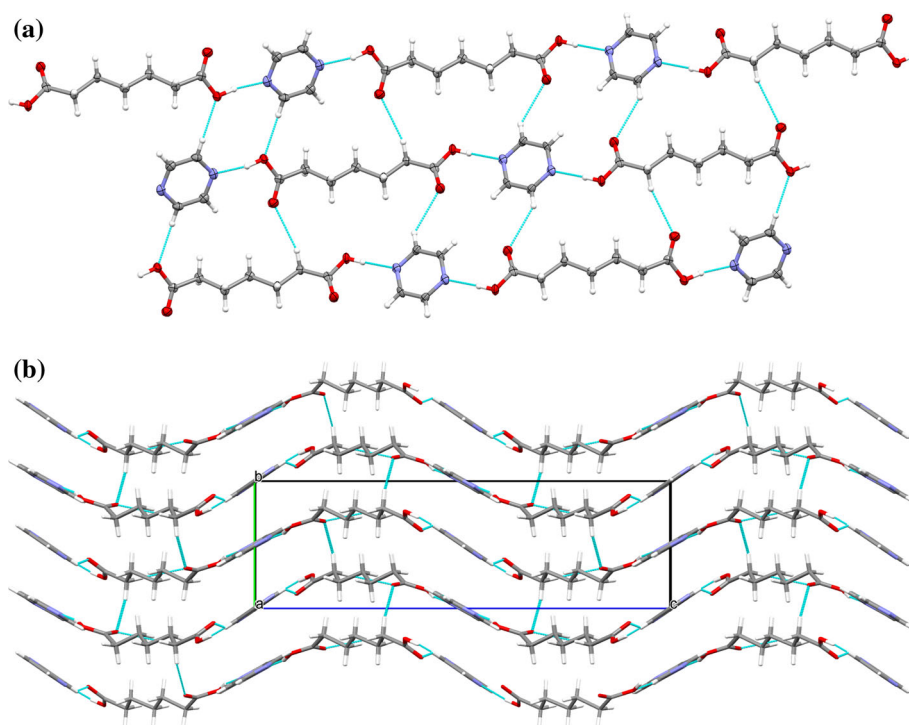


Fig. 10 A fragment of hydrogen-bonded chain of pyrazine and adipic acid molecules. The ellipsoids are drawn at the 50 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds

Fig. 11 a Hydrogen-bonded layer of pyrazine and pimelic acid; The ellipsoids are drawn at the 50 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds. **b** Fragment of the packing of crystals 6, as seen along [100] direction



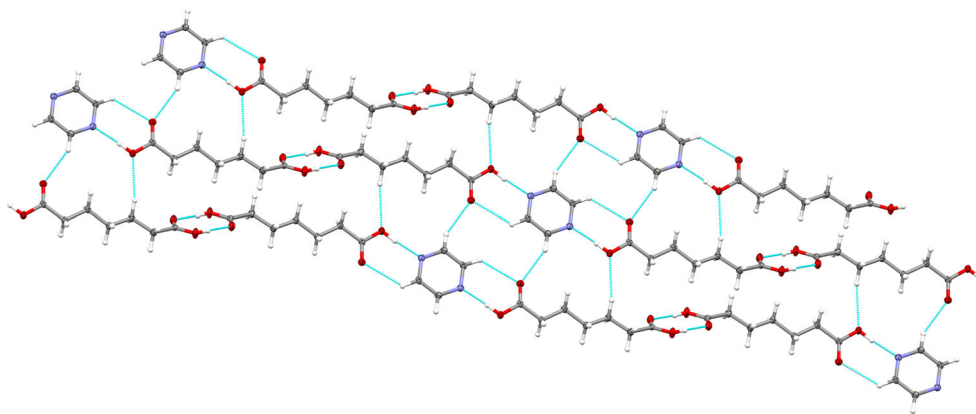
observed in **4** (where only one of these secondary contacts was classified as hydrogen bond) is still observed, but even the shorter C–H⋯O contact is longer than 2.75Å.

These chains are connected by means of relatively short C–H⋯O hydrogen bonds into wavy layers (Fig. 11a—ring

motifs $R_4^4(8)$, $R_3^3(16)$ and $R_3^3(17)$), which—in turn—lie one onto another and interact by weak contacts only (Fig. 11b).

In the 2:1 co-crystal, the asymmetric unit contains one acid molecule and half of— C_i —symmetrical pyrazine. It might be noted that contrary to **4a** the acid molecule also in

Fig. 12 A fragment of hydrogen-bonded chain of pyrazine and pimelic acid molecules. The ellipsoids are drawn at the 50 % probability level, hydrogen atoms are represented by *spheres* of arbitrary radii, and the *dashed lines* show the hydrogen bonds



this co-crystal is in all-*trans* conformation. As in the other 2:1 complexes, there are carboxylic acid hydrogen-bonded dimers which act as the elements of the chains with pyrazine molecules (Fig. 12). Secondary intra-chain C–H⋯O hydrogen bonds are very short here, and the inter-chain weak C–H⋯O hydrogen bonds make layers with similar graph-set combinations as in the case of **4a**: $R_4^2(10)$ and $R_4^4(30)$, the latter one larger because of the longer aliphatic chain.

Conclusions

In general, in the co-crystals (or molecular complexes) of pyrazine with the series of dicarboxylic acids with general formula (COOH)–(CH₂)_n–(COOH), where *n* ranges from 0 to 5, we have observed two principal packing modes:

- the chains of alternate pyrazine and acid molecules, connected by relatively strong and linear O–H⋯N hydrogen bonds. The conformation of these motifs can differ significantly, from flat ones to significantly twisted; depending on the dihedral angle between the terminal carboxylic group etc. Also, secondary C–H⋯O hydrogen bonds of different lengths can be sometimes observed within these principal motifs. Such layers are characteristic for 1:1 stoichiometry.
- the chains of hydrogen-bonded moieties which in these cases were pyrazine on one hand, but on the other hand—the carboxylic acid dimer (always centrosymmetric), created by homomolecular pairs of O–H⋯O hydrogen bonds. These motifs were found in the complexes with 2:1 acid: pyrazine ratio.

It has to be stressed that the co-crystals of the first type (1:1) were obtained (however, not always by the first try) for all the studied acids, while—despite many attempts with different ratios of reagents, solvents, methods etc.—we were not able to get the 2:1 co-crystals (actually, any

stoichiometry other than 1:1) for the acids with even number of CH₂ groups.

To rationalize this, we have tried to find another structural characteristics which might differ depending on the parity of the methylene groups, some of these parameters are listed in Table 3. In this series, certainly such a parameter is not the conformation of the carbon chain; in almost all cases it is all-*trans*, only for **4a** it is different (*trans-gauche*). Also, dihedral angles between the terminal COO planes could not serve as a good indicator, although there is a kind of rule: for all even diacids the carboxylic groups are almost (**1**) or exactly (**3**, **5**) coplanar, while for the odd ones there is no tendency, the COO groups can be almost coplanar (**4**), almost perpendicular (**2**, **2a**, **4a**) or somewhere between (**6**, **6a**).

Another hint is the symmetry of the diacid: when the number of methylene groups is even the molecule can have *C_i* symmetry, and it usually does (**3**, **5**); for odd number of CH₂ groups the available symmetries (*C₂*, *C_s*) are less favorable and harder to realize. Therefore, the realization of the packing with two centers of symmetry (for acid and hydrogen bond dimer) close one to each other can be difficult and it might be one of the reasons that the second packing mode (2:1) is not observed for even diacids.

Finally, the structural characteristics which correlates quite well with the parity of a number of CH₂ groups is the intramolecular (improper) torsion angle O=C⋯C=O. This angle is close to 180° for even and is spread between 8 and 88° for odd diacids. This is confirmed by the CSD analysis: Fig. 13 shows the distribution of the absolute values of the O=C⋯C=O torsion angles for even and odd number of methylene groups.

Supplementary data

Crystallographic data (excluding structure factors) for the structural analysis have been deposited with the Cambridge

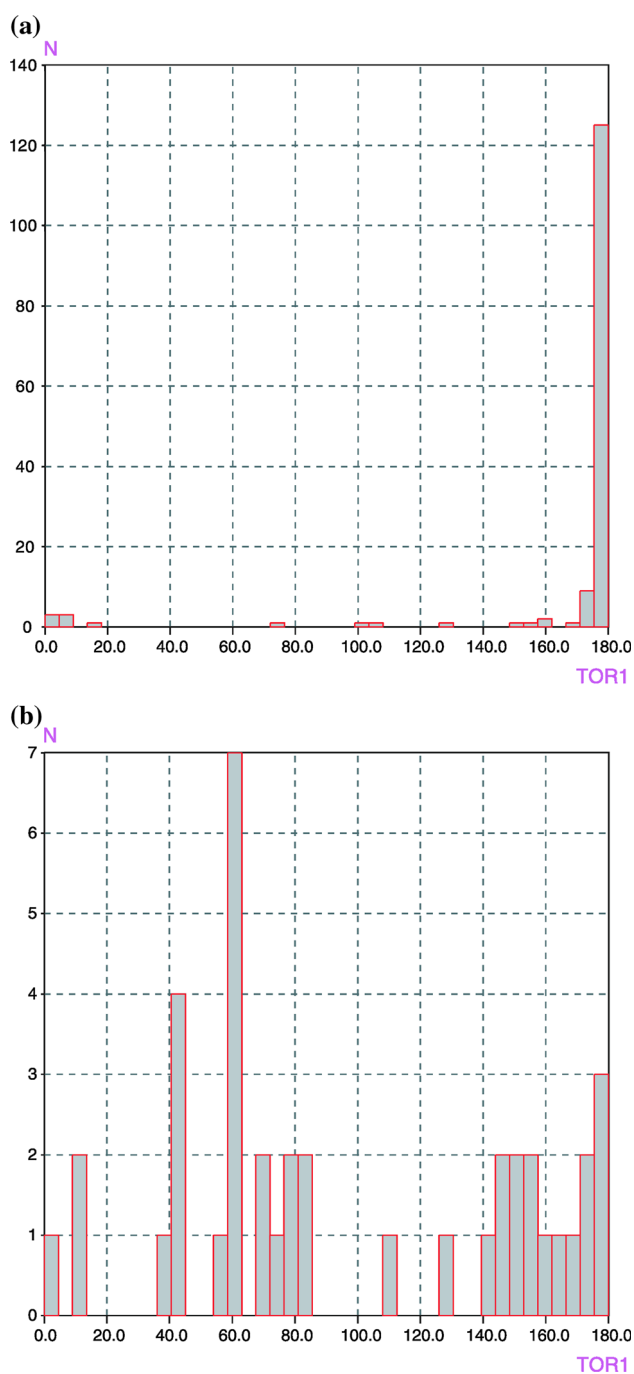


Fig. 13 Histograms for the absolute values of improper torsion angles $O=C\cdots C=O$ for even (*top*) and odd (*bottom*) numbers of methylene unit in the aliphatic chain of the diacid molecule

Crystallographic Data Centre, Nos. CCDC-924338-924346 (1–6a). Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. Fax: +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk, or www: www.ccdc.cam.ac.uk.

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