Hydrogen-bonded supramolecular structures in co-crystals of β- or ζ-diketone enols with 2,6-diaminopyridine or 2,4-diaminopyrimidine

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Preparation and single-crystal X-ray structure determination of five co-crystals of conjugated β- or ζ-diketoenolate anions (1,3-cyclopentanedionate, 1,3-cyclohexanedionate, 5-methyl-1,3-cyclohexanedionate and tropolonate) with aromatic protonated nitrogen bases (2,6-diaminopyridinium and 2,4-diaminopyrimidinium) are reported. Their packings are discussed in terms of the relative energies of the intermolecular hydrogen bonds formed, calculated by the Lippincott and Schroeder method, showing that such bonds largely determine the supramolecular net of interconnections within the crystal. The β- and ζ-diketoenolate anions are shown to have specific properties, being π-conjugated fragments with two terminal oxygens sharing a single negative charge that is partially displaced on one side or another according to the strength of the hydrogen bonds formed. The β-cyclohexanedionate anion displays, moreover, the ability to form a dimeric association with its neutral form through a very strong central [O–H···O]$^-$ bond of charge-assisted nature.

The design of new crystalline materials is mainly based on the synthesis of co-crystals formed by molecules having complementary intermolecular interactions.[1,2] The packing forces determining these intermolecular arrangements include a number of stronger or weaker non-covalent interactions[3] acting in complex co-operative or antagonist ways, which makes difficult, in most cases, the prediction of the crystal structures to be formed. Hydrogen bonds are normally dominant interactions,[4,5] which are expected to regulate mono-, bi- or tridimensional molecular architectures appearing systematically in crystals in connection with suitable molecular functional groups (supramolecular synthons[6]). Accordingly, it has often been possible to identify a number of structural patterns able to control intermolecular associations, which are important in many fields such as drug design and pharmacophore mapping, synthesis of supramolecular materials and crystal structure prediction.[7] Our present strategy consists in investigating couples of organic ions having multiple hydrogen bond donor and acceptor groups in order to form co-crystals whose supramolecular patterns can be more easily rationalized because the synergism of the H-bonds with the electrostatic forces between ions of opposite charges would dominate the network formation.[8–11] In this paper we explore the structures of co-crystals prepared by mixing β- or ζ-diketone enols with 2,6-diaminopyridines or 2,4-diaminopyrimidines. Neutral cyclic diketones, such as 1,3-cyclopentanedione, 1,3-cyclohexanedione and tropolone, enolize by forming π-delocalized diketone enols that produce, in crystals, infinite chains[12–14] connected by stronger than usual resonance-assisted hydrogen bonds (RAHB).[15,16] Because of the acidity of the enolic proton, however, these compounds are also able to donate a proton to organic bases, such as pyridine or pyrimidine derivatives, forming monomeric anions that fully delocalize the negative charge through the π-conjugated diketoenolate moiety. Both oxygens can thus become strong acceptors of multiple hydrogen bonds donated by diamino-pyridinium or -pyrimidinium cations that have accepted a proton from the enol, becoming potential donors of as many as five hydrogen bonds. Since the occurrence of multiple hydrogen bond donors and acceptors may interfere with the perfect balance of the intermolecular interactions, these crystals often include water molecules, as observed in 4 of the 5 cases presently reported. In some cases, the molecular arrangements around the conjugated diketoenolates give rise to characteristic patterns that can be considered as new supramolecular synthons.

Experimental

All reagents were purchased from Aldrich. Compounds **1**, **2** and **5** were obtained by crystallizing the two components in a 1 : 1 molar ratio from a mixture of water and ethanol. Compounds **3** and **4** were obtained by crystallizing the two components in a 2 : 1 molar ratio from a water–ethanol mixture for **3** and from acetonitrile for **4**.

Single crystal X-ray data for all co-crystals were collected on a Nonius-CAD4 diffractometer with monochromated Mo-Kα radiation ($\lambda = 0.7107$ Å) at room temperature. All intensities were corrected for Lorentz and polarization effects. The structures were solved using direct methods with the SIR92[17] program. Full-matrix least-squares refinement with anisotropic non-H atoms and isotropic hydrogens were performed on F^2 using the SHELXL-97[18] program. Details of crystal data collection and refinement are given in Table 1. All other calculations were accomplished using PARST.[19] Table 2 reports selected bond distances and Table 3 geometrical parameters of the intermolecular hydrogen bonds. ORTEP[20] views of the asymmetric unities are shown in Figs. 1(a)–5(a).

CCDC reference numbers 193879–193883. See http://www.rsc.org/suppdata/nj/b2/b205705k/ for crystallographic files in CIF or other electronic format.

Description of the structures

The molecules used in the synthesis of co-crystals **1**–**5** are sketched in Scheme 1 and crystals obtained are shortly described below.

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Table 1 Crystal data

Compound	**1**	**2**	**3**	**4**	**5**
Formula	$C_5H_5O_2{\cdot}C_5H_8N_3{\cdot}H_2O$	$C_5H_5O_2{\cdot}C_4H_7N_4{\cdot}H_2O$	$C_6H_8O_2{\cdot}C_6H_7O_2{\cdot}C_4H_7N_4{\cdot}H_2O$	$C_7H_{10}O_2{\cdot}C_7H_9O_2{\cdot}C_5H_8N_5$	$C_7H_5O_2{\cdot}C_5H_8N_3{\cdot}H_2O$
M	225.25	226.24	352.39	361.44	249.27
Crystal system	Monoclinic	Monoclinic	Triclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$ (N. 14)	$C2/c$ (N. 15)	$P\text{-}1$ (N. 2)	$P2/c$ (N. 13)	$P2_1/n$ (N. 14)
a/Å	7.394(2)	27.780(5)	8.642(2)	17.474(2)	10.376(3)
b/Å	19.603(2)	6.912(1)	10.132(2)	5.270(2)	17.697(2)
c/Å	8.107(1)	13.005(4)	10.721(5)	22.478(3)	14.647(3)
α/°	90	90	91.37(3)	90	90
β/°	94.56(1)	114.85(2)	92.95(2)	110.42(1)	109.23(2)
γ/°	90	90	106.66(2)	90	90
U/Å^3	1171.3(4)	2265.9(9)	897.4(5)	1939.9(8)	2539.5(9)
Z	4	8	2	4	8
T/K	296	296	296	296	296
μ/mm^{-1}	0.096	0.102	0.098	0.087	0.096
Measured reflections	3631	2852	4547	4348	7652
Unique reflections	3413	2726	4319	4231	7394
R_{int}	0.025	0.018	0.013	0.022	0.012
Observed reflections	2013	1967	2759	2124	4146
$R(F^2)$ (obs. reflns.)	0.0481	0.0453	0.0540	0.0622	0.0495
$wR(F^2)$ (all reflns.)	0.1350	0.1311	0.1731	0.1739	0.1348

1: Co-crystal $CPD^-{\cdot}DAPH^+{\cdot}H_2O$

The asymmetric unit of **1** consists of a 1,3-cyclopentanedionate anion (CPD^-), a 2,6-diaminopyridinium cation ($DAPH^+$) and a water molecule [Fig. 1(a)]. The O1 oxygen of the CPD^- group acts as a triple acceptor of hydrogen bonds, one from the protonated pyridinium nitrogen, one from the adjacent aminic group and the third one from a water molecule [Fig. 1(b)]. The N1–H···O1 hydrogen bond displays a rather short N1···O1 distance of 2.769(2) Å because it is assisted by the partial negative charge on O1 and positive charge on the N1–H group. Consistently, the second N3–H···O1 bond donated by the neutral aminic group displays a rather longer N3···O1 distance of 2.923(2) Å. Both the charged and neutral N–H···O bonds are slightly longer than those observed in squarate co-crystals[9] in relation with the fact that the O1 oxygen is a double acceptor of two hydrogen bonds where the two roughly parallel dipoles repeal each other (anticooperative hydrogen bonds[5]). Also, the O3–H···O1 hydrogen bond with water is rather short [O3···O1 distance of 2.675(2) Å], probably because of the partially negatively charged O1 oxygen. Oxygen O2 acts as a double hydrogen-bond acceptor, one donated by the second aminic group of the cation with a N2···O2 distance of 2.811(2) Å and the other by the water molecule. In the crystal packing, these interactions give rise to three-dimensional clusters built up by two cations and two anions arranged around a centre of symmetry and surrounded by eight water molecules [Fig.1(b)].

Table 2 Selected bond distances (Å)

1			
O1–C1	1.269(2)	C1–C2	1.377(2)
O2–C3	1.252(2)	C2–C3	1.396(2)
2			
O1–C1	1.262(2)	C1–C2	1.378(2)
O2–C3	1.252(2)	C2–C3	1.390(2)
3			
O11–C11	1.259(3)	O12–C12	1.245(3)
O31–C31	1.289(2)	O32–C32	1.311(2)
C11–C21	1.403(2)	C12–C22	1.420(2)
C21–C31	1.371(3)	C22–C32	1.343(3)
4			
O11–C11	1.247(3)	O12–C12	1.243(4)
O31–C31	1.290(4)	O32–C32	1.305(4)
C11–C21	1.397(4)	C12–C22	1.402(4)
C21–C31	1.366(4)	C22–C32	1.362(4)
5			
O11–C11	1.273(2)	O12–C12	1.267(2)
O21–C21	1.294(2)	O22–C22	1.265(2)
C11–C21	1.464(2)	C12–C22	1.473(2)
C11–C71	1.404(2)	C12–C72	1.402(2)
C21–C31	1.388(3)	C22–C32	1.410(2)
C31–C41	1.382(3)	C32–C42	1.374(3)
C41–C51	1.359(3)	C42–C52	1.357(3)
C51–C61	1.373(4)	C52–C62	1.378(3)
C61–C71	1.371(3)	C62–C72	1.385(3)

2: Co-crystal $CPD^-{\cdot}DAPMH^+{\cdot}H_2O$

The asymmetric unit of **2** consists of a 1,3-cyclopentanedionate anion (CPD^-), a 2,4-diaminopyrimidinium cation ($DAPMH^+$) and a water molecule [Fig. 2(a)]. Both oxygens of CPD^- act as acceptors of three hydrogen bonds [Fig. 2(b)]. The behaviour of oxygen O1 is similar to that observed in the previous structure **1,** being an acceptor of a strong hydrogen bond from the protonated nitrogen of the cation [N1···O1 = 2.739(2) Å], a weaker chelate one donated by the adjacent aminic group and a third one from a water molecule. The other oxygen O2 accepts two hydrogen bonds, N3–H···O2 and N4–H···O2, from aminic groups and a third one from a water molecule. According to a well known arrangement typical of 2-aminopyridines and 2-aminopyrimidines,[21] the $DAPMH^+$ cations form also H-bonded dimers disposed around a centre of symmetry by using one aminic group and the non-protonated N2 nitrogen. The crystal packing is characterized by tapes of alternate couples of anions and cations surrounded by water molecules [Fig. 2(b)].

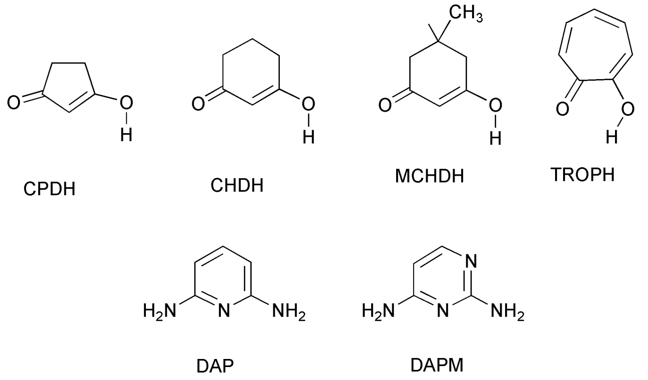
3: Co-crystal $CHDH{\cdot}CHD^-{\cdot}DAPMH^+{\cdot}H_2O$

The asymmetric unit of **3** is built up by an 1,3-cyclohexanedionate anion (CHD^-), a 2,4-diaminopyrimidinium cation ($DAPMH^+$), a neutral molecule of 1,3-cyclohexanedione enol (CHDH) and a water molecule [Fig. 3(a)]. The neutral CHDH

Table 3 Hydrogen bond parameters (Å and degrees)

D–H···A	D–H	D···A	H···A	∠D–H···A
1				
N1–H1···O1	0.91(2)	2.769(2)	1.91(2)	157(2)
N3–H32···O1	0.87(2)	2.923(2)	2.16(2)	146(2)
O3–H302···O1	0.90(2)	2.675(2)	1.80(2)	162(2)
N2–H21···O2^{i}	1.00(2)	2.811(2)	1.83(2)	166(2)
O3–H301···O2^{ii}	0.97(2)	2.705(2)	1.74(2)	171(2)
N2–H22···O3^{iii}	0.90(2)	2.986(2)	2.10(2)	171(2)
N3–H31···O3^{iv}	0.96(2)	2.886(2)	1.93(2)	173(2)
Symmetry codes: (*i*) 2 − *x*, −*y*, 1 − *z*; (*ii*) *x*, *y*, *z* + 1; (*iii*) 1 + *x*, *y*, *z*; (*iv*) *x*, 1/2 − *y*, *z* − 1/2.				
2				
N1–H1···O1	0.98(2)	2.739(2)	1.84(3)	152(2)
N3–H32···O1	0.80(3)	2.956(2)	2.29(2)	141(2)
O3–H301···O2	0.87(3)	2.767(2)	1.91(3)	166(3)
N3–H32···O2^{i}	0.80(3)	2.973(3)	2.54(3)	115(2)
N4–H42···O2^{ii}	0.93(2)	2.911(2)	1.99(2)	172(2)
N3–H31···N2^{iii}	0.99(2)	2.978(2)	2.01(3)	164(2)
N4–H41···O3^{iv}	0.88(3)	2.852(3)	1.99(3)	167(2)
O3–H302···O1^{v}	0.87(3)	2.763(2)	1.97(3)	151(3)
C8–H8···O3^{iv}	0.87(3)	3.486(3)	2.77(2)	140(2)
C9–H9···O3^{vi}	0.96(2)	3.483(3)	2.63(2)	142(2)
Symmetry codes: (*i*) 1/2 − *x*, 1/2 − *y*, −*z*; (*ii*) *x* − 1/2, 1/2 − *y*, *z* − 1/2; (*iii*) −*x*, *y*, −z − 1/2; (*iv*) *x* − 1/2, 1/2 + *y*, *z*; (*v*) 1/2 − *x*, −*y* − 1/2, −*z*; (*vi*) 1/2 − *x*, 1/2 + *y*, 1/2 − *z*.				
3				
O32–H32···O31	1.00(4)	2.470(3)	1.48(4)	173(3)
N3–H3···O11	0.95(2)	2.668(2)	1.73(2)	173(2)
O1–H12···O31	0.92(3)	2.776(3)	1.86(3)	174(3)
N2–H210···O12^{i}	0.85(3)	2.869(2)	2.25(2)	130(2)
N2–H220···N1^{ii}	0.83(3)	3.172(3)	2.35(3)	175(2)
N6–H61···O12^{iii}	0.85(2)	2.920(2)	2.09(2)	167(2)
N6–H62···O1^{iii}	0.90(2)	2.875(2)	1.98(2)	174(2)
O1–H11···O12^{iv}	0.90(4)	2.926(3)	2.05(4)	164(3)
C51–H511···O32^{v}	1.03(3)	3.486(4)	2.48(3)	166(2)
C62–H621···O11^{vi}	0.79(3)	3.397(3)	2.62(3)	168(3)
Symmetry codes: (*i*) *x* − 1, *y*, *z* − 1; (*ii*) −*x*, 1 − *y*, −*z*; (*iii*) 1 − *x*, 1 − *y*, 1 − *z*; (*iv*) 2 − *x*, 1 − *y*, 1 − *z*; (*v*) 2 − *x*, −*y*, −*z*; (*vi*) *x* + 1, *y*, *z* + 1.				
4				
O32–H32···O31	1.21(4)	2.455(3)	1.25(4)	170(4)
N1–H1···O11	0.90(3)	2.672(3)	1.81(3)	159(3)
N2–H201···O11	0.88(3)	2.912(4)	2.13(3)	147(3)
N6–H602···O12^{i}	0.99(5)	3.073(4)	2.15(5)	155(4)
N2–H202···O31^{ii}	0.91(4)	2.908(4)	2.04(4)	159(4)
N6–H601···O12^{iii}	0.82(4)	2.994(4)	2.24(3)	152(3)
C3–H3···O31^{ii}	0.98(3)	3.338(4)	2.56(3)	136(2)
C4–H4···O12^{iv}	0.99(3)	3.422(3)	2.55(2)	147(2)
Symmetry codes: (*i*) *x*, −*y*, *z* − 1/2; (*ii*) −*x*, *y* − 1, 1/2 − *z*; (*iii*) *x*, −*y* − 1, *z* − 1/2; (*iv*) −*x*, *y* − 2, 1/2 − *z*.				
5				
N11–H11···O21	0.87(2)	2.822(2)	2.02(2)	154(2)
N21–H211···O11	0.90(2)	2.851(2)	1.96(2)	173(2)
N31–H311···O21	0.93(2)	2.911(2)	2.08(2)	149(2)
N31–H312···O2	0.86(3)	3.028(3)	2.43(2)	127(2)
N12–H12···O21	0.90(1)	2.735(2)	1.86(1)	1.63(1)
N22–H221···O21	0.82(2)	3.091(2)	2.42(2)	139(2)
N22–H222···O12	0.89(2)	2.927(2)	2.07(2)	163(2)
N32–H321···O11	0.89(2)	2.937(2)	2.05(2)	174(2)
O1–H200···O11	0.82(3)	2.821(2)	2.01(3)	167(2)
O2–H300···O12	0.87(2)	2.769(2)	1.90(2)	175(2)
N21–H212···O1^{i}	0.92(3)	2.815(2)	1.90(2)	177(2)
O2–H400···O22^{ii}	0.87(2)	2.723(2)	1.91(2)	156(2)
N32–H322···O2^{iii}	0.89(2)	2.907(2)	2.03(2)	167(2)
O1–H100···O22^{iv}	0.87(2)	2.671(2)	1.80(2)	176(2)
C42–H42···O2^{v}	0.99(2)	3.412(2)	2.47(2)	159(2)
Symmetry codes: (*i*) 2 − *x*, −*y*, −*z*; (*ii*) 1 − *x*, −*y*, 1 − *z*; (*iii*) *x* + 1, *y*, *z*; (*iv*) 2 − *x*, −*y*, 1 − *z*; (*v*) 1/2 + *x*, −*y* − 1/2, 1/2 + *z*.				

and the anionic CHD^- are linked in couples by means of a strong O32–H···O31 bond having an O32···O31 distance of 2.470(3) Å. This belongs to the $[O–H\cdots O]^-$ class of negative-charge-assisted H-bonds [(−)CAHB][16] that, when perfectly symmetric, can become very strong with *d*(O···O) values down to 2.40 Å. Here, it is slightly dissymmetric and lengthened up to 2.470(3) Å because of the decrease of charge ($O–H\cdots O^{1/2-}$ instead of $O–H\cdots O^-$) and because its symmetry is broken by the rather strong O1–H···O31 interaction [O1···O31 = 2.776(3) Å]. The other charged oxygen, O11, is the acceptor of a strong $N^+–H\cdots O^{1/2-}$ bond from the protonated nitrogen of the $DAPMH^+$ cation, while the neutral



Scheme 1

oxygen O12 accepts three longer hydrogen bonds, two from different aminic groups and one from the water molecule. The hydrogen bond network consists of planar tapes of CHDH·CHD$^-$ dimers linked by dimeric DAPMH$^+$ cations in between. Water molecules connect two O31 and O12 oxygens belonging to upper and lower level tapes and, at the same time, make a N6–H···O1–H···O31 bridge between two molecules of the basal tape [Fig. 3(b)]. The in-plane O1–H···O31 hydrogen bond [O1···O31 = 2.776(3) Å] is stronger than the out-of-plane O1–H···O12 [O1···O12 = 2.926(3) Å], most probably because O31 is negatively charged while O12 is a formally neutral atom. The tapes are also linked, in the plane, by weak C51–H···O32 hydrogen bonds [Fig. 3(b)].

4: Co-crystal MCHDH·MCHD$^-$·DAPH$^+$

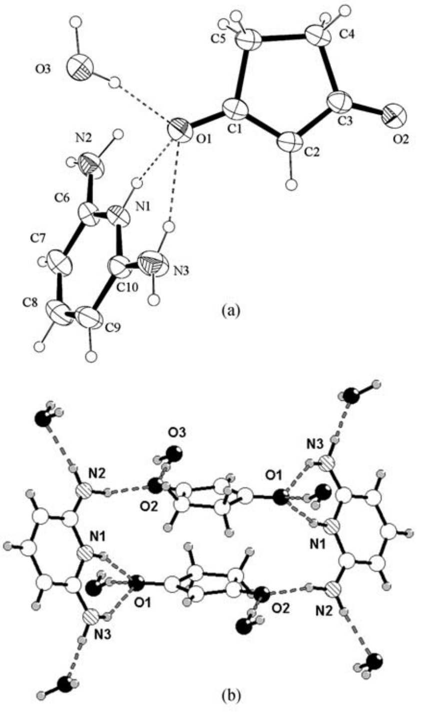


Fig. 1 (a) ORTEP view of the CPD$^-$·DAPH$^+$·H$_2$O complex **1** showing the thermal ellipsoids at 40% probability level. (b) The hydrogen-bonded cluster of CPD$^-$·DAPH$^+$ ions surrounded by water molecules formed by complex **1**.

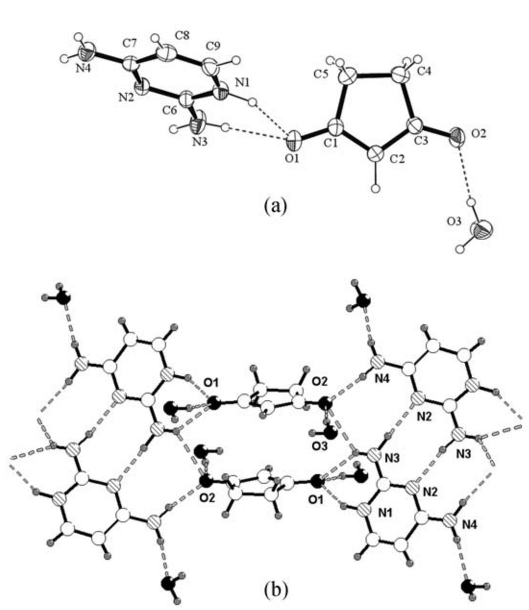


Fig. 2 (a) ORTEP view of the CPD$^-$·DAPMH$^+$·H$_2$O complex **2** showing the thermal ellipsoids at 40% probability level. (b) The hydrogen-bonded tape of CPD$^-$·DAPMH$^+$ ions surrounded by water molecules formed by complex **2**.

The asymmetric unit of **4** consists of a 5-methyl-1,3-cyclohexanedionate anion (MCHD$^-$), a 2,6-diaminopyridinium cation (DAPH$^+$) and a neutral molecule of 5-methyl-1,3-cyclohexanedione enol (MCHDH) [Fig. 4(a)]. As in **3** the MCHD$^-$ anion and the MCHDH are linked by means of a strong charge-assisted-hydrogen bond with an O32···O31 distance of 2.455(3) Å, which is almost perfectly proton-centred, O32···H = 1.21(4) Å and O31···H = 1.25(4) Å, because of

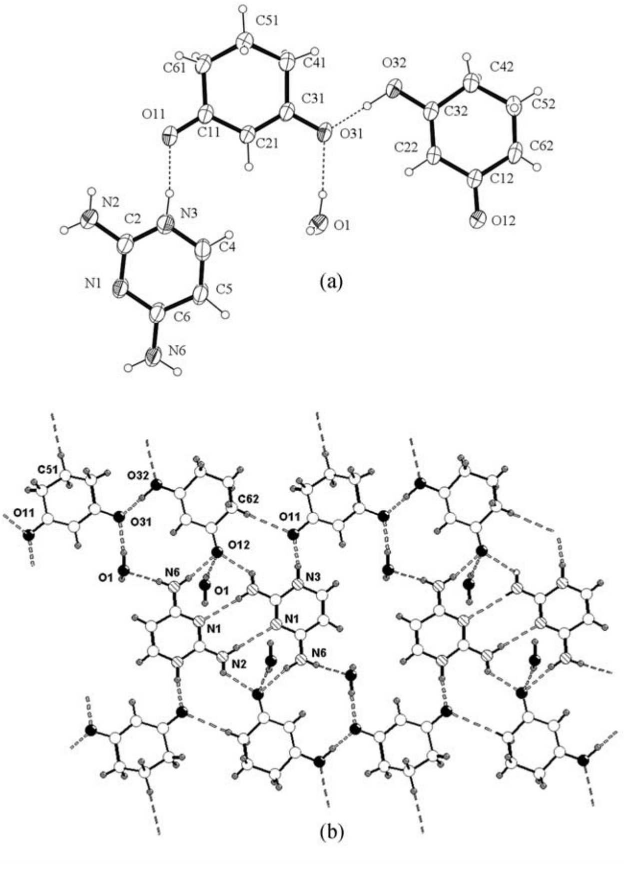


Fig. 3 (a) ORTEP view of CHDH·CHD$^-$·DAPMH$^+$·H$_2$O complex **3** showing the thermal ellipsoids at 40% probability level. (b) The hydrogen-bonded planar arrangement of CHDH·CHD$^-$·DAPMH$^+$·H$_2$O units formed by complex **3**.

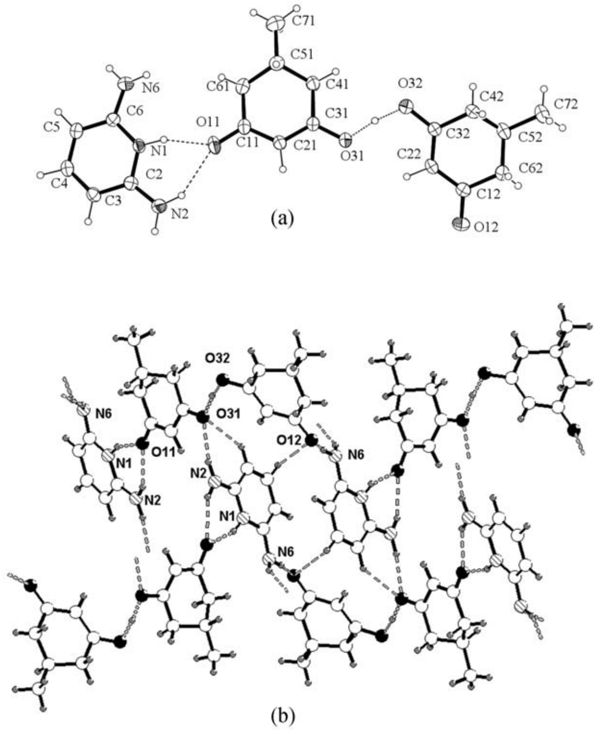


Fig. 4 (a) ORTEP view of the MCHDH·MCHD$^-$·DAPH$^+$ complex **4** showing the thermal ellipsoids at 40% probability level. (b) 3D hydrogen-bonded arrangement of MCHDH·MCHD$^-$·DAPH$^+$ units formed by complex **4**.

the resonance O–H···O$^{1/2-}$ ↔ O$^{1/2-}$···H–O. The resonance is confirmed by the fact that the two linked molecules, formally one neutral and one charged, display O11=C11–C21=C31–O31 and O12=C12–C22=C32–O32 heterodienic fragments with essentially identical bond lengths. The remarkable strength of the O32···H···O31 hydrogen bond may well be related to the weakness of the interleaving N2–H···O31 and C3–H3···O31 H-bonds. Also, the N1–H···O11 bond is of the charge-assisted (or charge-enhanced) type and, accordingly, is remarkably short [N1···O11 = 2.672(3) Å], while the chelate N2–H···O11 one is much longer [N2···O11 = 2.912(4) Å], being neutral and probably weakened by an anticooperativity effect.[5] O12 accepts two weak hydrogen bonds, one from an aminic group and the second one from an aromatic CH group.The three dimensional packing is shown in Fig. 4(b).

5: Co-crystal TROP$^-$·DAPMH$^+$·H$_2$O

The asymmetric unit of **5** consists of two tropolonate anions (TROP$^-$), two 2,4-diaminopyrimidinium cations (DAPMH$^+$) and two water molecules [Fig. 5(a)]. The TROP$^-$ anion can be considered, rather than a 1,2(or α)-diketoenolate, as a conjugated 1,7(or ζ)-diketoenolate where the π-delocalization involves all the bonds in the seven membered ring except C11–C21 and C12–C22 of the two independent anions.[12] The two TROP$^-$ anions display different intermolecular interactions. While O21 and O11 act as quadruple and triple acceptors, respectively, both O12 and O22 accept only two hydrogen bonds. It can be said that the first TROP$^-$ anion is captured by two DAPMH$^+$ cations: the O21 oxygen accepts two rather strong hydrogen bonds from the protonated nitrogens N11 and N12 [N11···O21 = 2.822(2) Å, N12···O21 = 2.735(2) Å] and two weaker chelate ones from the neutral aminic groups, while O11 accepts two hydrogen bonds from aminic groups and one from a water molecule. Each oxygen of the second independent TROP$^-$ anion accepts two hydrogen bonds,

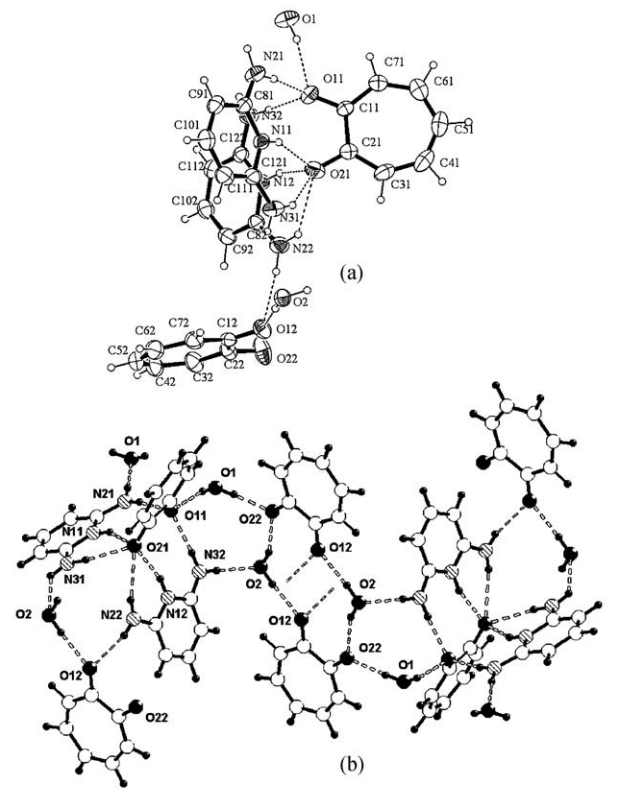


Fig. 5 (a) ORTEP view of the TROP$^-$·DAPMH$^+$·H$_2$O complex **5** showing the thermal ellipsoids at 40% probability level. (b) 3D hydrogen-bonded arrangement of TROP$^-$·DAPMH$^+$·H$_2$O units formed by complex **5**.

O12 from a water molecule and from an amino group and O22 from two water molecules. Because of the different co-ordination of the two anions, the packing shown, in part, in Fig. 5(b) does not display the formation of any regular supramolecular pattern.

Discussion and conclusions

Structural features of π-conjugated diketoenolate anions

Π-Conjugated diketoenolates are organic anions able to share the negative charge on both the oxygens and to delocalize the π electrons through the heterodienic system [O–C=C–C=O]$^-$ in **1**, **2**, **3** and **4**, and [O–C=C–C=C–C=C–C=O]$^-$ in **5**. In CPD$^-$ anions (co-crystals **1** and **2**) C–C and C–O couples of bonds display almost equivalent distances, which corresponds to an almost perfect π-delocalization of the entire fragment, slight asymmetries being imputable to the different contacts of the terminal oxygens with the environment. Accordingly, the longer C–O distances [1.269(2) in **1** and 1.262(2) Å in **2**] are on the side where the stronger charge-assisted N$^+$–H···O$^{1/2-}$ bonds are pointing to, while the other N–H···O$^{1/2-}$ and O–H···O$^{1/2-}$ bonds donated by neutral aminic groups and water molecules seem unable to produce C–O bonds longer than 1.252(2) Å.

The perturbing effects of charge-assisted N$^+$–H···O$^{1/2-}$ bonds on C–O length is confirmed in compound **5**. Here, one single negatively charged O21 oxygen is an acceptor of two strong N$^+$–H···O$^{1/2-}$ hydrogen bonds and, accordingly, its C–O bond is lengthened up to 1.294(2) Å while the three oxygens, which make weaker hydrogen bonds with neutral aminic groups or water molecules, are associated with significantly shorter C–O distances of 1.26–1.27 Å.

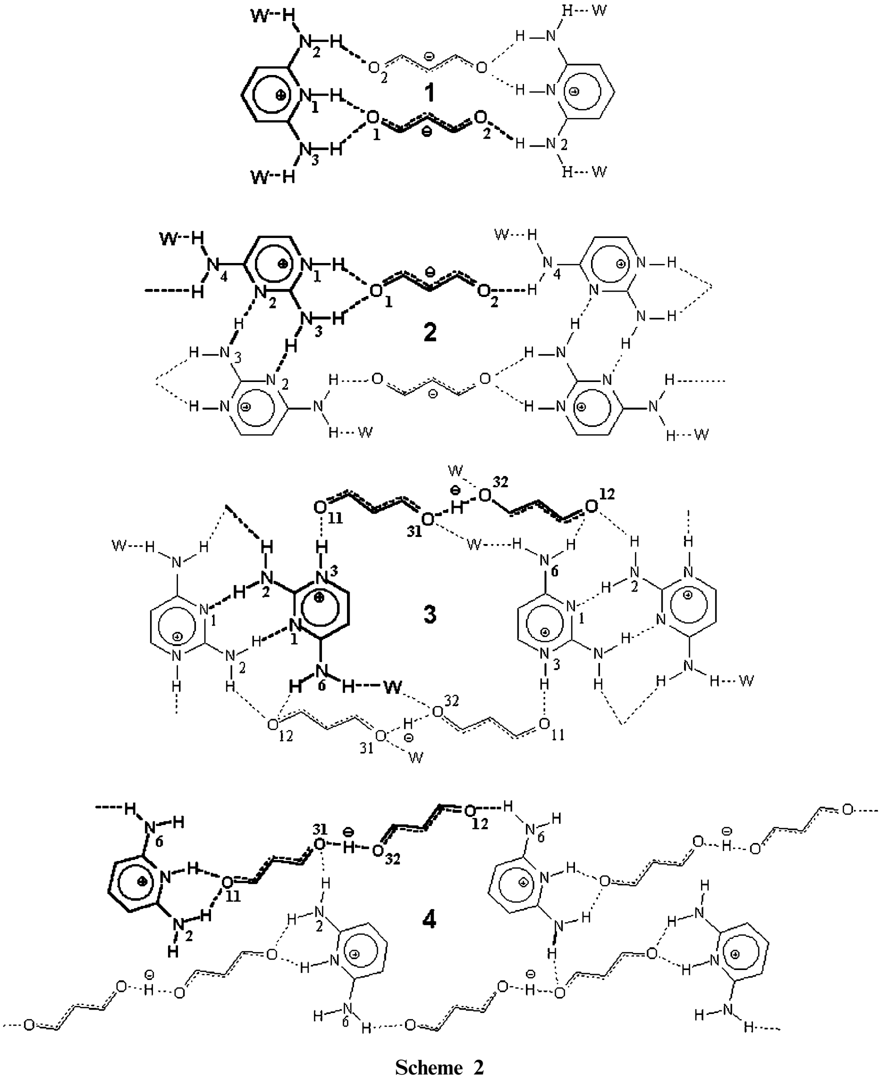
Co-crystals **3** and **4** contain also β-diketone enol – β-diketoenolate complexes linked by very short O–H···O$^{1/2-}$ hydrogen bonds, with $O\cdots O$ distances of 2.46–2.47 Å. These strong bonds of $[O–H\cdots O]^-$ nature produce a localization of the enolate negative charge on the two central oxygens with consequent lengthening of the central C31–O31 bonds [1.289(2) Å in **3** and 1.290(4) Å in **4**] with respect to the sidewise C11–O11 one [1.259(3) Å in **3** and 1.247(3) Å in **4**]. The symmetry between C31–O31 and C32–O32 distances [C32–O32 = 1.311(2) Å in **3** and 1.305(4) Å in **4**] and the almost centred position of the proton, particularly in **4**, confirm that these bonds can actually be considered as three-center-four-electron covalent bonds resulting from the $[O–H\cdots O]^- \leftrightarrow [O\cdots H–O]^-$ resonance.[16] The charge concentration on the central oxygens can account for the fact that the $N^+–H\cdots O^{1/2-}$ interactions, in spite of being remarkably short in **3** and **4** as they were in **1** and **2**, become unable to lengthen the corresponding C–O distances [1.259(3) in **3** and 1.247(3) Å in **4**]. The trimeric association enol-enolate-protonated base observed here matches the recently reported trimolecular complexes observed in the co-crystals among *p*-nitrobenzoic acid, *p*-nitrobenzoate anion and pyridinium cations.[22]

Supramolecular organization

In a series of previous papers[8–10] we have analyzed a number of packings of co-crystals consisting of an organic acid (squaric acid and 1,3-dimethylbarbituric acid) transmitting a proton to an aromatic base and then forming ionic couples linked by $N^+–H\cdots O^-$ bonds. Data collected agree in indicating that H-bond acceptors are saturated by donors "in order of decreasing strength of the H-bonds formed" and the order found was $[O–H\cdots O]^- > N^+–H\cdots O^{1/2-} > N–H\cdots O^{1/2-} > N–H\cdots O$. These same criteria can be used to rationalize the packing of the present compounds (Scheme 2) with the exception of compound **5**, where the tropolonate anion has two very close H-bond acceptors ($O\cdots O$ = 2.57 Å), which generate a negative field strong enough to attract *two* diaminopyridinium cations, so hindering any regular disposition of positive and negative ions in the crystal.

H-bond energies, E_{HB}, have been estimated according to the semi-empirical method of Lippincott and Schroeder,[23] which gives E_{HB} for a generic $X–H\cdots Y$ bond as a function of the $X\cdots Y$ distance and X–H–Y angle, $E_{HB} = f[d(X\cdots Y), \alpha(X–H–Y)]$. When applied to compounds **1**–**4**, it gives the following energy ranges: $[O–H\cdots O]^-$ in **3** and **4**: $-E_{HB}$ = 15–16 kcal mol^{-1}; $N^+–H\cdots O^{1/2-}$ *plus* chelated $N–H\cdots O^{1/2-}$: $-E_{HB}$ = 3–4 kcal mol^{-1} in **1** and **2** and ≅6 kcal mol^{-1} in **3** and **4**; $N–H_2\cdots O^{1/2-}$ in **1**–**4**: $-E_{HB}$ = 1–3 kcal mol^{-1}. The dimerization free energy of two 2,4-diaminipyrimidinium cations in **2** and **3** can be estimated to be in the range $-\Delta G$ = 5–8 kcal mol^{-1}, obtained by summing up their $-E_{HB}$ value (1–3 kcal mol^{-1}) with an entropic $-T\Delta S$ term of some 4–5 kcal mol^{-1} at room temperature, arising from the smaller decrease of entropy occurring when molecular association is coupled with chelation (chelate effect).[24]

It may be thought that the formation of a crystal within the solvent (in this case a water–ethanol mixture or acetonitrile) is controlled by the kinetics of its nucleation, the first nuclei being formed when the concentrations (or populations) of



Scheme 2

the species constituting the crystal exceed by some amount the solubility of the crystal itself (sovrasaturation). Though all H-bond interactions are known to be severely damped by the presence of water as a solvent, the nature of the species present in solution can still be guessed from the order of the energy terms given above. The list of the species most likely to be present in solution (not in order of probability) is as follows:

(*i*) $DAPH^+$ monomers in **1** and **4**; (*ii*) $(DAPMH^+)_2$ dimers in equilibrium with the monomers in **2** and **3**, of which the former is to be preferred in view of the previous considerations; (*iii*) monomeric CPD^- in **1** and **2**, CHD^- in **3** and $MCHD^-$ in **4** in equilibrium with their H-bonded complexes with the corresponding neutral enol $CPDH{\cdot}CPD^-$, $CHDH{\cdot}CHD^-$ and $MCHDH{\cdot}MCHD^-$; (*iv*) complexes of the protonated $DAPH^+$ and $DAPMH^+$ bases with the monomeric CPD^-, CHD^- and $MCHD^-$ or dimeric $CPDH{\cdot}CPD^-$, $CHDH{\cdot}CHD^-$ and $MCHDH{\cdot}MCHD^-$ anions connected through the moderately strong $N^+–H\cdots O^{1/2-}$, often supported by the chelated $N–H\cdots O^{1/2-}$ one; (*v*) water molecules.

In spite of their complexity, all crystal packings observed in **1**–**4** [Figs. 1(b)–4(b)] can be reduced to H-bond-driven associations of the most probable species among the molecular entities listed above, as shown graphically in Scheme 2. In **1** the $DAPH^+{\cdot}CPD^-$ complex has two H-bond functionalities left out, the aminic N2H and the enolate $O2^{1/2-}$, which could complete the structure by forming dimers as well as chains. In **1** the dimer is chosen, while the remaining N2H and N3H groups are saturated by water molecules. Conversely, the $DAPH^+{\cdot}MCHDH{\cdot}MCHD^-$ complex in **4**, which has the same unsaturated H-bond donor and acceptor groups (N6H and $O12^{1/2-}$), forms double chains linked by $N6–H\cdots O12$ bonds, which are kinked and fit kink-to-hole in tridimensional arrays interconnected by $N2–H\cdots O31$ bonds (see **4** of Scheme 2). In **2** and **3** the $(DAPMH^+)_2$ dimer dominates the packing. Its association with CPD^- in **2** and $CHDH{\cdot}CHD^-$ in **3** leaves unsaturated the terminal $O^{1/2-}$ atom (O2 in **2** and O12 in **3**) of the anion and the *para*-NH_2 group (N4 in **2** and N6 in **3**) of the complex. In **2** the cation-anion couples associate in chains, giving rise to a ribbon made up of two antidromic centrosymmetric chains where the remaining functionalities (N4–H) are saturated by waters. In **3** the $DAMH^+{\cdot}CHDH{\cdot}CHD^-$ complex again forms a ribbon where, however, the *p*-aminopyrimidine group is vertical instead of being horizontal as in **2**. As before, the remaining N–H groups appear to be saturated by water molecules, which make a bridge to the O31 and O32 atoms at the centre of the anionic dimer.

The present analysis seems therefore to indicate that a relevant part of the intermolecular association topology can be rationalized starting from an estimate of the most probable bimolecular complexes classed according to their H-bond interaction energies integrated, when needed, by entropic considerations. Perhaps this analysis could be carried a little further. For instance, we have not discussed the fact that, though $CPDH{\cdot}CPD^-$ and $CHDH{\cdot}CHD^-$ (or $MCHDH{\cdot}MCHD^-$) anions seem to have the same *a priori* probability of being formed, the former is never observed (**1** and **2**) while the latter occurs twice (**3** and **4**) in the rather curious conformation of one-third of the hexagonal ring found by Etter *et al.*[25] in the β-cyclohexanedione enol–benzene complex. This behaviour is understandable, however, because 1,3-cyclohexanedione is a stronger acid than 1,3-cyclopentanedione (pK_a in water of 4.34 and 5.23, respectively[26]) and thus imputed to form stronger $[O–H\cdots O]^-$ bonds.

Moreover, it is known from previous studies on β-chains,[13,14] which are chains of β-diketone enols connected by resonance-assisted–hydrogen-bonds, that CPDH chains are only of the simple translational type while CHDH ones can assume six different conformations, which would add to the CHDH dimer in solution a free enthalpy advantage of $RT \ln 6 = 1.1$ kcal mol^{-1} (at 25 °C) over the CPDH one. This is probably the reason why it has proved impossible to crystallize a 1 : 1 mixture of CHDH [or MCHDH] and DAP [or DAPM] in spite of all attempts while crystallization of the 2 : 1 mixtures has successfully given co-crystals **3** and **4**.

Present considerations seem to indicate that a rather detailed understanding of the *topology* of intermolecular associations can actually be obtained on the grounds of a rational knowledge of the molecular interactions involved. This statement, however, raises two orders of considerations. The first, and the basic one for crystal engineering, is whether the present *a posteriori* rationalization could be reversed into an *a priori* prediction. The second is that the prediction of the intermolecular association is far less, anyway, than a true *ab initio* prediction of the stable crystal structure, which would require one to know the exact matching of all complementary chemical functionalities (*e.g.*, hydrogen bonding, charge transfer or dipolar interactions) and of the overall shapes of the interacting bodies (van der Waals interactions).

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