Competition between hydrogen bonding and donor–acceptor interactions in co-crystals of 1,3-dimethylbarbituric acid with aromatic amines

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In contrast to cyclohexane-1,3-diones, 1,3-dimethylbarbituric acid (DMBA) does not enolize in crystals with formation of infinite H-bonded chains. Conversely, it forms crystals that completely lack traditional H-bond donors and hence are held together by C–H···O H-bonds and $C^{\delta+}{=}O^{\delta-}\cdots C^{\delta+}$ interactions of a putative donor–acceptor nature. In view of these specific features, the DMBA molecule appeared to be a good candidate to study the competition of the various intermolecular forces in its co-crystals with traditional H-bond donors such as *o*-nitrophenylhydrazine, *p*-nitroaniline, 2,6-diamino-4-phenyl-1,3,5-triazine, 2,6-diaminopyridine and *p*-aminopyridine. X-Ray crystallographic results are analyzed in terms of crystal packing forces and formation of specific packing *leitmotifs* (supramolecular synthons). The conclusions indicate that, though a rational crystal engineering of co-crystals is far from being accomplished, a reasonable rationalization of the complex intermolecular forces acting in competition in the crystal packing is henceforth achievable.

Intermolecular interactions are the basis for crystal engineering, their nature and strength determining their competitive importance in forming different crystal packings.[1] Among these intermolecular forces hydrogen bonds are the most important in view of their higher energy and directionality.[2] These properties have been extensively utilized in the planning of crystal adducts of molecules or ions having complementary acceptor and donor sites.[3] It has been observed that the strength of these directional forces, and then their ability to control the formation of intermolecular aggregates, depend on the nature and polarity of the donor and acceptor groups and become very high when the hydrogen bond is assisted by resonance[4] or by charge.[5] The three dimensional network in a crystal is determined by other forces as well, such as multipolar electrostatic, donor–acceptor and van der Waals interactions.[6] Often, the weaker C–H···X (X = O, N) hydrogen bonds also act as cooperative forces in stabilizing the net formed by stronger hydrogen bonds also involving oxygen and nitrogen atoms as donors which may be competitive, with respect to traditional hydrogen bonds, aiding in the formation of the crystal adducts.[7]

1,3-Dimethylbarbituric acid (DMBA) was originally chosen as the building block or tecton[1c] of infinite chains linked by strong O–H···O resonance-assisted H-bonds (RAHB)[4a,d] on the grounds of our previous findings that practically all cyclopentane- and cyclohexane-1,3-diones, and 1,3-diethyl-2-thiobarbituric acid[8] readily enolize and give the predicted chains. DMBA, however, proved impossible to enolize in all solvents tested, even those of very low polarity. Non-enolized DMBA, however, turned out to form very interesting crystals whose packing was dominated, because of the lack of traditional H-bond donors, by perpendicular donor–acceptor C=O···C=O interactions[6b,d] and C–H···O hydrogen bonds.[7] In view of the specific features of DMBA, it was decided to attempt its co-crystallization with a number of H-bond donors, mostly amines, aimed to substitute donor–acceptor with H-bond interactions, as well as to promote the diketone enolization by increasing the crystal environment basicity. Accordingly, this paper reports the preparation and crystal structure determination of DMBA (**1**) and of its adducts DMBA · *o*-nitrophenylhydrazine (**2**), DMBA · *p*-nitroaniline (**3**), DMBA · 2,6-diamino-4-phenyl-1,3,5-triazine (**4**), DMBA · 2,6-diaminopyridine (**5**) and 5′-hydroxy-5,5′-bi(DMBA) · *p*-aminopyridine (**6**).

Description of the structures

The molecules studied are sketched in Scheme 1 and are indicated by upper case (**A** and **B**) or lower case (**a**–**e**) letters according to their prevalent H-bond acceptor or donor nature. Preparative and X-ray crystallographic details for the six compounds investigated are reported in the Experimental. Table 1 reports the geometrical parameters of the intra- and intermolecular contacts and Fig. 1–6 show their most characteristic packing arrangements.

DMBA (1) A complex

Because DMBA does not have any traditional H-bond donor group, molecules interact in the crystal by means of C–H···O=C hydrogen bonds. Fig. 1(a) shows that the DMBA units are linked in chains by C2–H···O3 contacts (H···O3 = 2.38 Å) that are strictly comparable to the strongest C–H···O bonds formed with carbonyls by Cl_3C–H [average H···O of 2.31(1) Å] and –C≡C–H [average H···O of 2.40(2) Å],[7d] in agreement with the acidic nature of the $>C2H_2$ methylene group surrounded by two carbonyls. These chains are, in turn, transformed into two-dimensional arrays by weaker $C6H_3\cdots O1$ and $C5H_3\cdots O2$ interactions having an average H···O of 2.67 Å (Table 1). These C–H···O bonded planes are connected by nearly perpendicular $C^{\delta+}{=}O^{\delta-}\cdots C^{\delta+}{=}O^{\delta-}$ interactions of a plausible donor-acceptor nature [Fig. 1(b)]: C3=O2···C1 (C···O = 2.99 Å) on one side of the ring and C4=O3···C1 and C4=O3···C4 (C···O of 3.18 and 3.11 Å, respectively) on the other side. The three contacts are all well below the sum of the C and O van der Waals radii of 3.22 Å[9] and are to be compared with an

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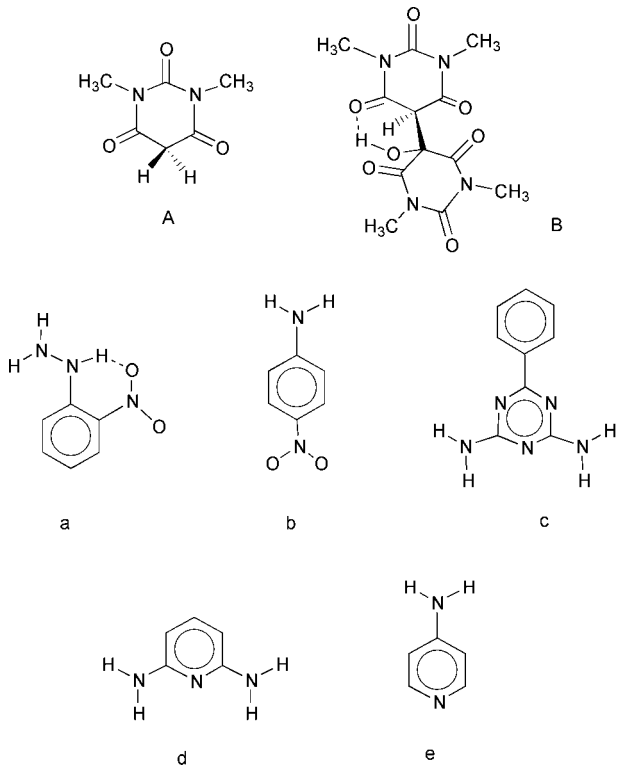


Scheme 1

average of *ca.* 3.4 Å and a minimum of some 2.8 Å found for this type of interaction.[6b] Strictly similar interaction patterns are observed in the crystal structure of 1,3-diethylbarbituric acid [Fig. 1(c)],[10] in spite of the completely different packing arrangement.

DMBA·*o*-nitrophenylhydrazine (2), A·a complex

The insertion of a molecule having three N–H H-bond donors substantially modifies the scheme of the interactions. The crystal structure consists now of rows of DMBA and 2-nitrophenylhydrazine molecules [Fig. 2(a)] held together in ribbons by means of N–H···O bonds complemented by C–H_3···O interactions. The ribbons are held in planes by C9–H···O3 hydrogen bonds and the planes are interconnected up and down through dipole–dipole interactions [Fig. 2(b)] between the C3=O2 carbonyl of DMBA and the N5–O4 moiety of the nitro group of 2-nitrophenylhydrazine (O4···C3 = 3.11, O2···N5 = 3.14 Å) and by C2–H···O1 bonds [Fig. 2(c)] linking dimers of DMBA molecules (H···O = 2.76 Å). The N3–H moiety of the hydrazinic group forms bifurcated hydrogen bonds, one intramolecular (N3···O5 = 2.61 Å) and the second intermolecular with the O1 oxygen of DMBA (N3···O1 = 2.88 Å), which is rather short in spite of the bifurcation that should weaken both H-bonds formed,[11] this strengthening can be accounted for in terms of increased N–H acidity caused by the *o*-nitro substituent. The apical NH_2 unit of the hydrazinic moiety forms two chelated and rather weak hydrogen bonds with the same O2 of DMBA (N4···O2 = 3.07 Å).

DMBA·*p*-nitroaniline (3), A·b complex

The *p*-nitroaniline adds a bifurcated N–H_2 donor and a nitro H-bond acceptor. Interestingly, it uses most of its H-bonding potentialities to form a chain of *p*-nitroanilines held together by H-bonds between its aminic and nitro functions (Fig. 3) this is a well-recognized supramolecular synthon already identified in other papers[1a,12] and appears to have a remarkable stability in spite of the rather weak H-bonds formed (average

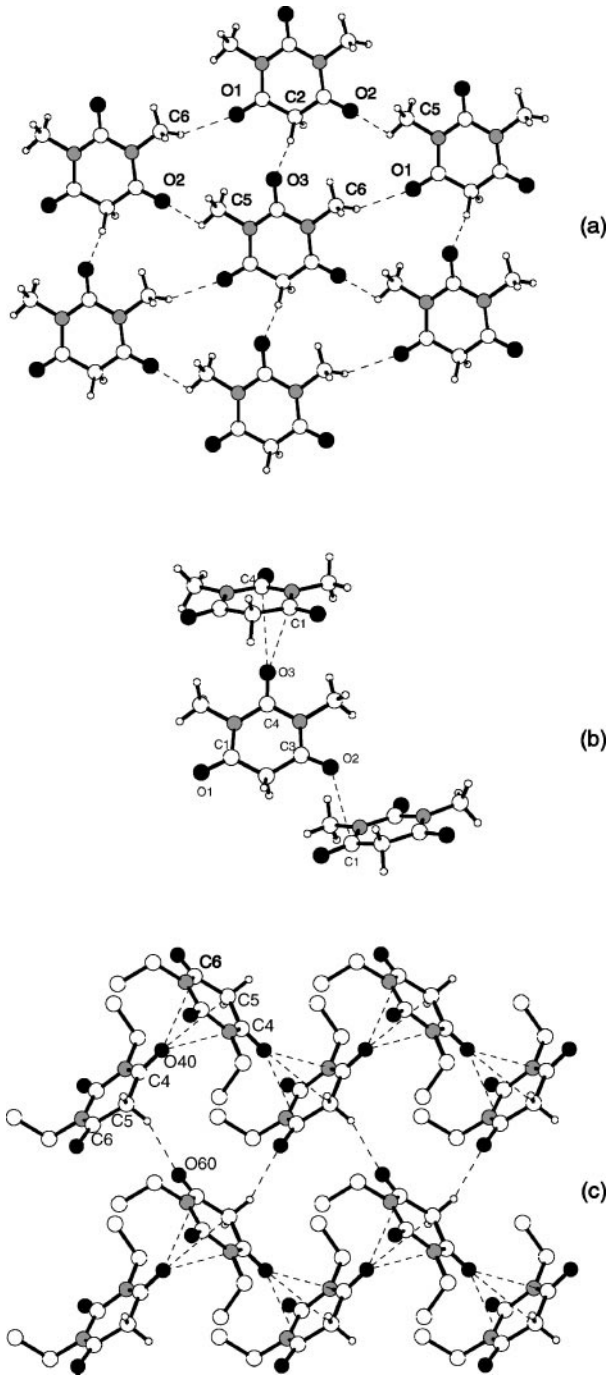


Fig. 1 (a) Layer of DMBA molecules of compound **1** linked by C–H···O interactions; (b) electrostatic donor–acceptor C=O···C=O interactions involving carbonyl groups of DBMA molecules; (c) C–H···O and C=O···C=O interactions in the crystal packing of 1,3-diethylbarbituric acid.[10]

N···O = 3.19 Å). On both sides of the chain, DMBA molecules bind by forming N3–H···O3 H-bonds by using the other N–H of the aminic function and leaving unoccupied every other position which can now accomodate a second DMBA molecule linked by chelated H-bonds: C11–H···O1 and C12–H···O2 (average H···O = 2.61 Å). The result is a planar sheet that is stacked with other similar ones through a dimeric C2–H···O1 (H···O = 2.64 Å) interaction identical to that reported in Fig. 2(c) for **2**.

DMBA·2,6-diamino-4-phenyl-1,3,5-triazine (4), A·c complex

In this crystal structure, the asymmetric unit consists of two molecules of DMBA and two molecules of 2,6-diamino-4-phenyl-1,3,5-triazine. The asymmetric unit has now eight N–H

Table 1 Geometrical parameters (Å and degrees) with e.s.d.s in parentheses for hydrogen bonding and other molecular interactions with contact distances shorter than the sum of the van der Waals radii

D–H···A	D–H	H···A	D···A	D–H···A	X–D···A	D···A	X–D···A
1 = A							
C2–H21···O3^{i}	0.93(5)	2.38(5)	3.303(4)	170(4)	C4–O3···C1^{iv}	3.184(4)	118.8(3)
C5–H51···O2^{ii}	0.96	2.78	3.476(4)	130	C4–O3···C4^{iv}	3.114(4)	161.6(3)
C6–H62···O1^{iii}	0.96	2.56	3.132(4)	118	C3–O2···C1^{v}	2.986(4)	115.3(3)
Symmetry codes: *i*: *x*, *y*, *z* + 1; *ii*: *x* − 1/2, *y*, *z* + 1/2; *iii*: *x* + 1/2, *y*, *z* + 1/2; *iv*: 1 − *x*, 1/2 − *y*, *z* − 1/2; *v*: 1/4 + *x*, 1/4 − *y*, 1/4 + *z*.							
2 = A · a							
N3–H30···O5^{i}	0.82(3)	2.00(3)	2.609(3)	130(3)	N5–O4···C3^{v}	3.108(3)	90.4(3)
N3–H30···O1^{i}	0.82(3)	2.22(2)	2.877(3)	138(3)	C3–O2···N5^{v}	3.136(3)	89.8(3)
N4–H410···O2^{ii}	0.82(2)	2.68(4)	3.067(3)	111(3)			
N4–H420···O2^{ii}	0.88(4)	2.71(3)	3.067(3)	106(3)			
C9–H9···O3^{iii}	0.92(2)	2.54(2)	3.305(3)	138(2)			
C2–H21···O1^{iv}	0.94(2)	2.76(2)	3.252(40)	114(2)			
C5–H53···O2^{ii}	0.92(3)	2.60(7)	3.262(40	130(5)			
Symmetry codes: *i*, *x*, *y*, *z*; *ii*: *x* − 1, *y*, *z*; *iii*: *x*, *y* − 1, *z* − 1; *iv*: 1 − *x*, 1 − *y*, 1–*z*; *v*: 1 − *x*, 1 − *y*, −*z*.							
3 = A · b							
N3–H31···O3^{i}	0.80(3)	2.16(3)	2.949(3)	167(3)			
N3–H32···O4^{ii}	0.89(3)	2.34(3)	3.221(3)	168(3)			
N3–H32···O5^{ii}	0.89(3)	2.48(3)	3.168(3)	134(3)			
C2–H21···O2^{iii}	0.93(2)	2.64(2)	3.462(3)	149(2)			
C12–H12···O1^{iv}	0.94(2)	2.61(2)	3.216(3)	123(2)			
C11–H11···O1^{iv}	0.90(2)	2.62(2)	3.202(3)	123(2)			
Symmetry codes: *i*: *x*, *y*, *z*; *ii*: 1 − *x*, 1/2 + *y*, 1/2 − *z*; *iii*: −*x*, 1 − *y*, −1 − *z*; *iv*: 1 + *x*, *y*, 1 + *z*.							
4 = A · c							
N61–H612···O11^{i}	1.02(5)	2.20(5)	3.192(5)	164(4)	C41–O31···C42^{vii}	3.083(5)	159.0(3)
N61–H611···O12^{i}	1.01(4)	2.12(4)	3.108(5)	162(3)	C41–O31···N22^{vii}	3.030(4)	160.2(3)
N71–H711···O22^{ii}	0.94(4)	2.05(4)	2.982(5)	170(3)			
N62–H621···O32^{iii}	0.83(4)	2.01(4)	2.958(5)	167(4)			
N71–H712···N32^{i}	0.90(3)	2.26(3)	3.132(4)	163(3)			
N62–H622···N51^{i}	0.89(4)	2.20(4)	3.049(4)	160(4)			
N72–H721···N52^{iv}	0.77(4)	2.31(4)	3.048(4)	161(4)			
N72–H722···N42^{v}	0.89(4)	2.13(4)	3.011(4)	167(4)			
C21–H212···O21^{vi}	0.92(4)	2.46(4)	3.361(5)	166(4)			
Symmetry codes: *i*: *x*, *y*, *z*; *ii*: *x* − 1, *y*, *z*; *iii*: *x*, *y* − 1, *z*; *iv*: 1 − *x*, 1/2 + *y*, 1/2 − *z*; *v*: 1 − *x*, *y* − 1/2, 1/2 − *z*; *vi*: −*x*, −*y*, −*z*; *vii*: 1 − *x*, 1 − *y*, −*z*.							
5 = A · d							
N3–H30···O2^{i}	0.92(2)	1.87(2)	2.717(2)	153(1)			
N4–H410···O2^{i}	0.92(2)	2.02(2)	2.841(2)	147(2)			
N5–H510···O1^{ii}	0.93(2)	1.96(2)	2.883(2)	171(2)			
N5–H520···O1^{iii}	0.90(2)	1.99(2)	2.851(2)	158(2)			
N4–H420···O3^{iv}	0.89(2)	1.97(2)	2.858(2)	174(2)			
Symmetry codes: *i*: *x*, *y*, *z*; *ii*: 1 − *x*, −*y*, −*x*; *iii*: *x* + 1, *y*, *z* + 1; *iv*: *x*, *y* − 1, *z*.							
6 = B · e							
O42–H42···O11^{i}	0.87(2)	1.76(2)	2.579(2)	156(2)	C31–O21···N22^{i}	3.008(1)	109.6(1)
N1–H1···O21^{i}	0.91(2)	1.83(2)	2.713(1)	162(2)	C31–O21···C32^{i}	2.788(1)	83.4(1)
N2–H21···O11^{ii}	0.90(3)	2.17(3)	3.054(2)	165(2)	C31–O21···C12^{i}	3.203(2)	77.2(1)
N2–H21···O12^{ii}	0.90(3)	2.71(3)	3.059(2)	104(2)	C22–O42···C42^{v}	2.812(2)	140.0(1)
N2–H22···O31^{iii}	0.92(4)	2.34(3)	3.080(3)	137(2)			
C2–H2···O31^{iii}	0.96(3)	2.55(2)	3.198(2)	125(1)			
C4–H4···O22^{iv}	0.92(3)	2.49(2)	3.262(2)	142(2)			
C4–H4···O42^{iv}	0.92(3)	2.57(2)	3.405(3)	152(2)			
C5–H5···O11^{iv}	0.94(2)	2.66(2)	3.320(2)	128(2)			
C51–H521···O32^{vi}	0.90(3)	2.77(3)	3.086(2)	102(2)			
C51–H531···O32^{vi}	1.00(4)	2.80(5)	3.086(2)	97(3)			
Symmetry codes: *i*: *x*, *y*, *z*; *ii*: *x*, *y* + 1, *z* + 1; *iii*: *x*, *y* + 1, *z*; *iv*: −*x*, −*y*, 1 − *z*; *v*: −*x*, −*y*, −*z*, *vi*: *x*, *y* − 1, *z*.							

moieties as H-bond donors on four NH_2 groups, six N≡ aromatic acceptors, and six more DMBA carbonyls as acceptors. The resulting packing is extremely complex but can be understood, at least for our limited aims, from Fig. 4(a). One of the two triazine molecules makes an H-bonded ribbon (N72–H···N42: N···N = 3.01; N72–H···N52: N···N = 3.05 Å), again a well-known supramolecular synthon.[13] The second triazine molecule binds to both sides of the ribbon through N–H···N≡ bonds (N62–H···N51: N···N = 3.05; N71–H···N32: N···N = 3.13 Å) assuming, however, a position nearly perpendicular to the ribbon plane. In these connections four N–H groups have been engaged, leaving four others free for binding to a corresponding number of C=O DMBA oxygens [Fig. 4(b) and Table 1] (N62–H···O11: N···O = 3.19; N61–H···O12: N···O = 3.11; N62–H···O32: N···O = 2.96; N71–H···O22: N···O = 2.98 Å). This net of interconnections leaves out four acceptors [Fig. 4(a) and 4(b)], the two N31 and N41 atoms, which remain unsaturated, and the two DMBA carbonyls C31=O21 and C41=O31. The first makes the centrosymmetric C–H···O dimer already observed in structures **2** and **3** [Fig. 2(c)] while the second makes the donor–acceptor interaction [Fig. 4(c)] already observed in **1** [Fig. 1(b)].

DMBA · 2,6-diaminopyridine (5), A · d complex

In this crystal structure, enolization occurs and a hydrogen is transferred from the DMBA methylene to the pyridine nitro-

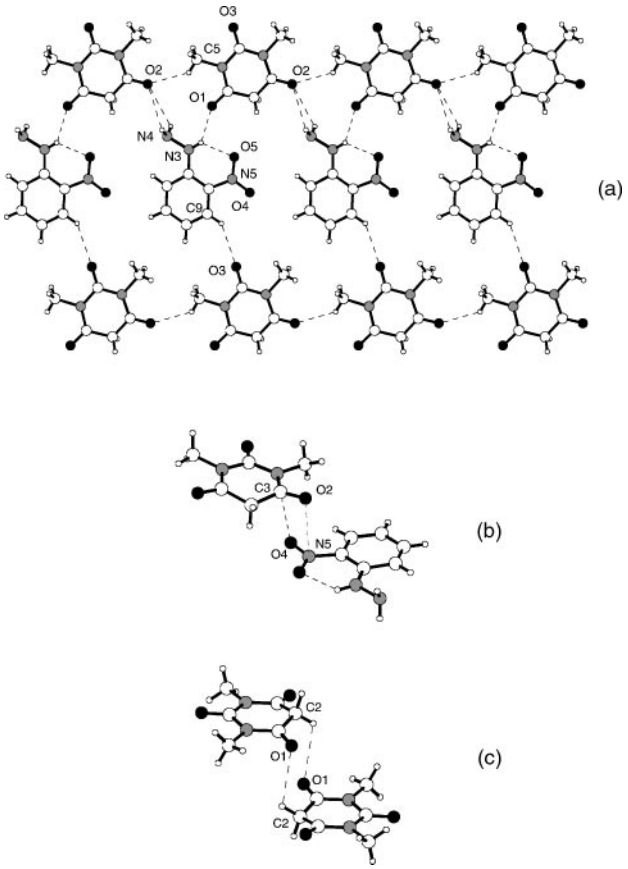


Fig. 2 (a) Layer of molecules of complex **2** (DMBA · *o*-nitrophenylhydrazine) linked by N–H···O and C–H···O hydrogen bonds; (b) dipole–dipole interactions between the carbonyl C3=O2 of DMBA and the N5–O4 moiety of the nitro group of *o*-nitrophenylhydrazine; (c) dimeric C–H···O interaction involving the acidic methylene group $C2H_2$ and the carbonyl C1=O1.

gen with formation of an ionic couple. The resulting packing is essentially ionic (CsCl type) with a coordination number of eight around both anions and cations. The donor–acceptor balance can now be summarized as follows: five N–H donors (one $\equiv NH^+$ and two $-NH_2$ groups) and three oxygens as acceptors (one C4=O3 carbonyl and the C1–$O1^{1/2-}$ and C3–$O2^{1/2-}$ groups on the β-diketoenolate moiety). Accordingly, two oxygens must become acceptors of two H–bonds each, and the third of just one, as actually found in Fig. 5.

(HBI-DMBA)·*p*-aminopyridine (6), B·e complex

The crystal structure is an aggregation of an unexpected condensation product of DMBA, that is 5′-hydroxy-5,5′-bis-DBMA (HBI-DBMA), with *p*-aminopyridine. One of the two DMBA moieties is enolized with transfer of one methylene

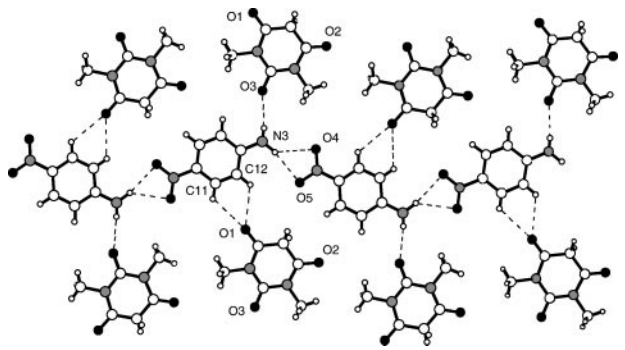


Fig. 3 Layer of molecules of complex **3** (DMBA · *p*-nitroaniline) linked by N–H···O and C–H···O hydrogen bonds.

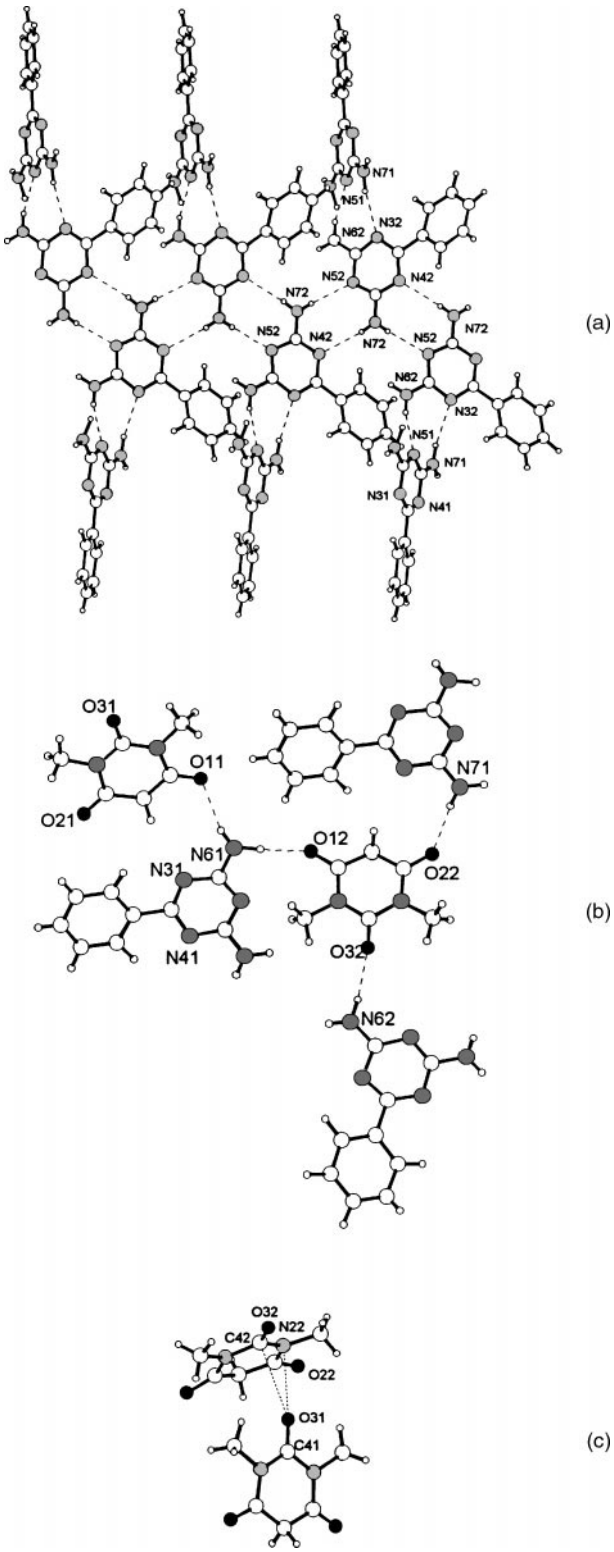


Fig. 4 (a) Molecular ribbon of complex **4** (DMBA · 2,6-diamino-4-phenyl-1,3,5-triazine) generated by molecules of 2,6-diamino-4-phenyl-1,3,5-triazine; (b) N–H···O interactions between molecules of DMBA and 2,6-diamino-4-phenyl-1,3,5-triazine; (c) donor–acceptor C=O···C/N interactions between molecules of DMBA.

proton to the pyridine nitrogen; the entire molecule is in a conformation fixed by the intramolecular O42–H···O11 bond and by the donor–acceptor interactions O21···N22 (3.01 Å), O21···C12 (3.20 Å) and O21···C32 (2.79 Å). The protonated *p*-aminopyridine is the donor of three NH···O bonds that are all formed [Fig. 6(a)] with the enolized moiety of HBI-DMBA. The N–H^+···$O^{1/2-}$ bond is stronger (N1–H···O21: N···O = 2.71 Å) than the H-bonds formed by the neutral

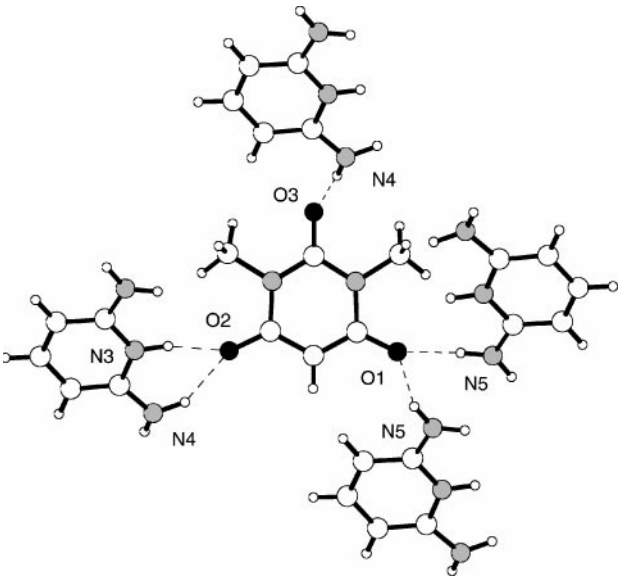


Fig. 5 The N–H···O hydrogen bond arrangements between the two ions for the complex **5** ($DMBA^- \cdot$ 2,6-diaminopyridinium$^+$).

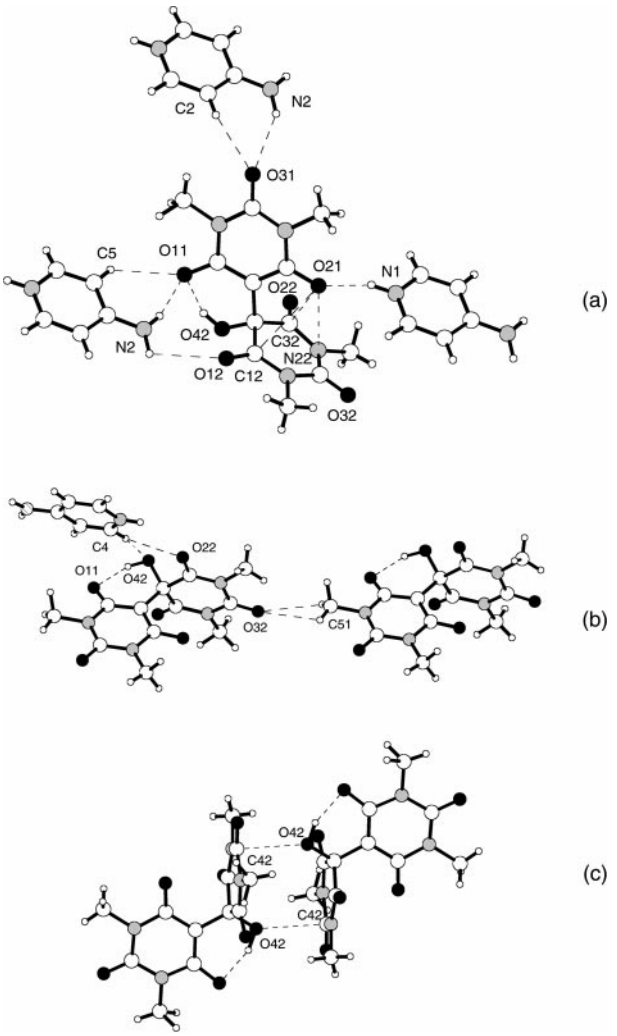


Fig. 6 (a) View of the ionic complex **6** (HBI-$DMBA^- \cdot$ *p*-aminopyridinium$^+$) showing the intramolecular electrostatic donor–acceptor interactions between the enolate O21 oxygen and the two carbonylic carbons C12 and C32, and nitrogen N22, and the N–H···O hydrogen bond arrangements between the two ions which, in two cases, are supported by C–H···O interactions; (b) simple C–H···O interactions; (c) donor–acceptor interactions between the hydroxyl O42 and C42 atoms.

amine group, which are substantially weaker (N2–H···O31, N2–H···O11 and N2–H···O12: N···O in the range 3.05–3.08 Å) despite being supported by two other weak C–H···O interactions. Having now used all the N–H donors to saturate the acceptors of the first DMBA subunit, the second one is compelled to interact in other ways through its four H-bond acceptors (the three carbonyls C12=O12, C32=O22, C42=O32 plus the O42 of the hydroxyl group). Only O12 is an acceptor of a weak N2–H···O12 H-bond, the other oxygens being involved in C–H···O bonds [Fig. 6(b)] or in a twin $>O^{\delta-}\cdots C^{\delta+}$ donor–acceptor interaction (O42···C42 = 2.81 Å), which is one of the shortest contacts of this type so far reported[6b] [Fig. 6(c)].

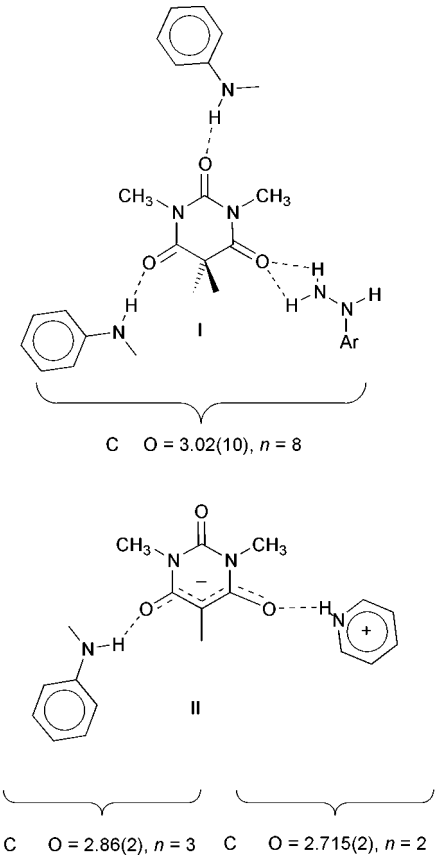
Discussion and conclusions

A first point to discuss is why DMBA does not enolize its β-diketone moiety to give the expected RAHB-bonded chains[4a,d] typical of all pentane- and hexane-1,3-diones and of the parent compound 1,3-diethyl-2-thiobarbituric acid, a behaviour shared by very few other β-diketones (among which the well-known case of 1,3-indandiones)[14] and most probably due to their unfavourable enolization energies. Accordingly, these have been evaluated, as energy differences between the enolized and non-enolized forms, by quantum mechanical calculations performed with GAUSSIAN98[15] at the DFT B3LYP/6-31G(d,p) level of theory for both energy and full geometry optimization. Molecules were assumed to have planar and the OH group of the enolic form to be in its *syn* conformation with respect to the C=C double bond. No zero point corrections were applied. The energies of the enols are calculated to be systematically higher than those of the diketone forms, and the corresponding enolization energies to increase in the order 1,3-cyclohexanedione, 1,3-cyclopentanedione, 1,3-dimethyl-2-thiobarbituric acid, DMBA and 1,3-indanedione, being 0.72, 0.84, 8.95, 10.96 and 11.64 kcal mol^{-1}, respectively. With respect to a β-diketone crystal, the corresponding crystal of the β-diketone enol form is then destabilized because of the loss of its enolization energy but stabilized by the formation of the infinite O–H···O RAHB-bonded chains (β-chains). The H-bond energy has been evaluated[4d] to be of the order of 7–15 kcal mol^{-1} for a series of crystals forming such O–H···O β-chains. Therefore, the order of the calculated enolization energies is consistent with the fact that only DMBA and 1,3-indandione do not undergo enolization, though the energy balance is such that it cannot exclude that the enolic forms of these molecules will be, in the end, crystallized, as actually happens for diethylthiobarbituric acid, which forms one of the strongest intermolecular O–H···O resonant H-bonds so far known (O···O = 2.455 Å; $E_{HB} \simeq 15.5$ kcal mol^{-1}).[4d,10]

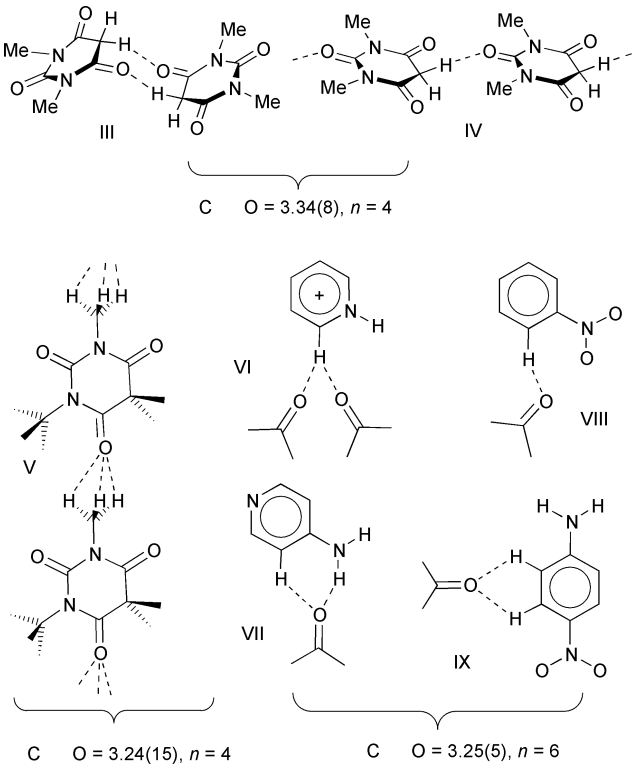
Considering now the crystal packings of the compounds studied, two different factors must be accurately distinguished. The first is our putative ability to predict the actual packings by simple chemical intuition, and present findings clearly show that this aim cannot be reasonably pursued. The second concerns our degree of chemical understanding of molecular interactions, that is of the forces that determine the packing itself and the rest of this paper will show that, in this respect, the situation appears to be much more encouraging. For the sake of simplicity, the discussion is partitioned by type of molecular interaction: (i) traditional H-bonds that, in the present case, are N–H···O and, in one case, N–H···N bonds; (ii) C–H···O H-bonds, (iii) $C^{\delta+}=O^{\delta-}\cdots C^{\delta+}$ donor–acceptor interactions and (iv) the possible role played by cooperative packing *leitmotifs* (periodic supramolecular synthons)[1a].

Traditional H-bonds

A summary of the N–H···O bonds formed by all the com-



Scheme 2



Scheme 3

pounds studied is reported in Scheme 2. They are chemically distinguishable into four different groups: (i) aromatic $\equiv N^+$–H···$^{1/2-}$O–C (II; structures **5** and **6**); (ii) aminic $>N$–H···$^{1/2-}$O–C (II; structures **5** and **6**); (iii) aminic and hydrazinic $>N$–H···O=C (I; structures **2**, **3**, **4**, **5** and **6**); and (iv) a single case of a three-centred hydrazinic interaction ArN(H)–NH_2···O=C (I, structure **2**). It is generally recognized that the strongest N–H···O bonds are of the type N^+···O^- with matching of the pK_a values of the H-bond donor and acceptor groups. These bonds are traditionally called *salt bridges*[2b] and more recently, low barrier H-bonds (LBHB)[16] or (+/−) charge-assisted H-bonds [(+/−) CAHB].[4c,17] According to expectation, the strongest H-bonds presently observed are of the (+/−) CAHB type between the protonated pyridine and the enolate of the DBMA β-diketone group [II, group (i)] with an average N···O distance of 2.715(2) Å, while those having only a charged acceptor [II, group (ii)] and the neutral ones [I, group (iii)] are progressively weaker with average N···O distances of 2.86(2) and 3.02(10) Å, respectively. However, no reason can be presently suggested for the fact that the secondary amine function, Ar–NH–NH_2, of the hydrazinic moiety seems able to produce shorter N–H···O=C$<$ bonds with an N···O distance of 2.877 Å (structure **2**).

C–H···O H-bonds

Only in structure **5** are all H-bond acceptors saturated by traditional N–H donors. In the others, the donor–acceptor balance requires the formation of C–H···O and donor–acceptor interactions, the former being collected in Scheme 3. All C–H···O interactions involve a DMBA carbonyl as acceptor and, with the sole exception of VIII (where the C–H···O is in simple support of a normal N–H···O bond), the C–H groups implied are always chosen among the most acidic ones, in agreement with previous considerations on the role played by C–H acidity in determining the strength of C–H···O bonds.[7d,18] This is particularly true for the methylene of DMBA, which is so acidic as to impart the name barbituric acid, and it is the constituent of two well-defined supramolecular synthons in the form of dimers (III; structures **2**, **3** and **4**) or catemers (IV; structure **1** and 1,3-diethylbarbituric acid[10]), but it is also true for VI, VII and IX where the C–H used is *ortho* to either a N^+–H or to a NO_2 group. Finally, in V the two *ortho* carbonyls promote unusual acidic properties in the normally inert N-methyl group, and induce the formation of chains of DBMA molecules in **1**, **2** and **6** through a rather uncommon –CH_3···O=C interaction [average C···O = 3.24(15) Å] previously observed in the analogous compound trimethylisocyanurate.[19]

$C^{\delta+}$=$O^{\delta-}$···$C^{\delta+}$ donor–acceptor interactions

Interactions between two carbonyls in molecular crystals have recently been reviewed by Allen and coworkers[6b] who have shown that they are of two different types. The first is an antiparallel matching of two C=O groups that is to be classified as a pure dipole–dipole interaction; the second is the nearly perpendicular C=O···C=O interaction displayed in Fig. 1(b), 4(c) and 6(c). In the present structures, no antiparallel C=O dipolar interactions are found, presumably because the trigonal disposition of carbonyls in DMBA wipes out the total molecular dipole moment [the only interaction of this type observed is that between a C=O and the N–O of a nitro group, shown in Fig 2(b)]. Perpendicular $N^{\delta-}$···$C^{\delta+}$=$O^{\delta-}$ interactions have been extensively studied[20] in connection with the incipient nucleophilic addition of aminic nitrogen to carbonyl, which is observed in some molecular crystals. They are normally classified as charge-transfer or donor–acceptor interactions because the full range of C–N distances from van der Waals contacts to true C–N bonds is observed, together with a relevant carbonyl pyramidalization caused by the nitrogen approach. The present perpendicular C=O···C=O interactions could be, at least formally, classified as nucleophilic additions of oxygen, instead of nitrogen, to the electrophilic carbonyl carbon. They

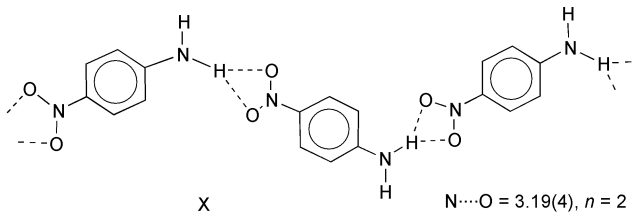
Table 2 Crystal data, data collection and refinement for **1**–**6**

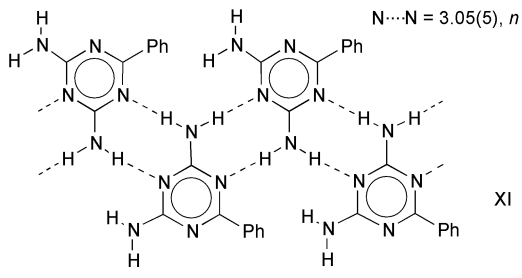
Formula	**1** $C_6H_8N_2O_3$	**2** $C_6H_8N_2O_3 \cdot C_6H_7N_3O_2$	**3** $C_6H_8N_2O_3 \cdot C_6H_6N_2O_2$	**4** $C_6H_8N_2O_3 \cdot C_9H_9N_5$	**5** $C_6H_8N_2O_3 \cdot C_5H_7N_3$	**6** $C_{12}H_{14}N_4O_7 \cdot C_5H_2N_2$
M	156.14	309.29	294.27	686.71	265.28	420.39
Crystal system	Orthorhombic	Triclinic	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group	$Fdd2$	$P\bar{1}$	$P2_1/c$	$P2_1/c$	$P\bar{1}$	$P\bar{1}$
a/Å	15.642(3)	8.181(2)	7.586(2)	11.223(1)	7.262(1)	10.111(2)
b/Å	29.006(6)	12.891(2)	16.547(2)	7.226(2)	9.466(3)	11.747(2)
c/Å	6.556(1)	7.758(2)	10.856(2)	40.737(5)	9.839(1)	9.369(2)
α/°	90	104.73(2)	90	90	91.28(2)	107.72(1)
β/°	90	116.10(2)	97.10(2)	90.53(1)	109.46(1)	109.668(1)
γ/°	90	73.34(2)	90	90	94.01(2)	66.16(1)
U/Å^3	2974.5(9)	696.0(3)	1352.3(5)	3303.5(1)	535.4(2)	940.0(3)
Z	16	2	4	4	2	2
T/K	296	296	296	296	296	296
μ/cm^{-1}	1.13	1.17	1.15	1.01	1.04	1.18
Unique reflns.	957	3026	2943	6435	2765	4524
R_{int}	0.026	0.013	0.017	0.019	0.012	0.009
Obs. reflns. $[I > 2\sigma(I)]$	628	1947	1759	3539	2079	3840
R (obs. reflns.)	0.046	0.048	0.053	0.066	0.041	0.040
wR (all reflns.)	0.126	0.135	0.147	0.203	0.116	0.116

have, however, remarkably different features. The oxygen never approaches the carbon to less than about 2.80 Å, a distance that is shorter by only 0.40 Å than the van der Waals contact of 3.22 Å, while the accepting carbonyl is never pyramidalized in a sensible way. This may suggest that these $C^{\delta+}{=}O^{\delta-}\cdots C^{\delta+}$ interactions are at the very limit of charge transfer and, for practical purposes, preferably classifiable as closed-shell electrostatic interactions.

Cooperative packing *leitmotifs*

One of the main open questions of crystal engineering is whether there are specific packing patterns (supramolecular synthons) associated with some specific molecules or molecular fragments (tectons) that may "ensure generality and reproducibility"[1a] in our attempts at crystal design. Though this is not the kind of question that can be answered on the grounds of the few present structures, there are actually two cases (structures **3** and **4**; Scheme 4) that seem to support the efficacy of supramolecular synthons in determining the overall crystal packing. In fact, *p*-nitroaniline and 2-aminotriazine (part of the 2,6-diamino-4-phenyl-1,3,5-triazine molecule in **4**) are well known to form in their crystals, or in crystals of their derivatives, typical patterns in the form of chains (X)[12] and ribbons (XI)[13], respectively, and exactly these motifs are found in co-crystals **3** and **4**, in spite of the presence of the co-existing DMBA molecules.





Scheme 4

Experimental

All reagents were purchased from Aldrich. Compounds **2**–**5** were obtained by crystallizing the two components in a 1 : 1 molar ratio from the appropriate solvent. Compound **1** was recrystallized from toluene, while co-crystals **2**, **3** and **5** were crystallized from a mixture of diethyl acetate and THF, and **4** and **6** from methanol. Co-crystal **6** turned out to be an unexpected complex obtained by crystallizing DMBA with 4-aminopyridine in hot methanol in which DMBA has undergone oxidative dimerization with formation of 5′-hydroxy-5,5′-bis(DMBA).

All X-ray diffraction data were collected at room temperature, **1** on a Nonius Kappa CCD diffractometer and **2**–**6** on an Enraf-Nonius CAD-4 diffractometer using graphite-monochromated Mo-Kα radiation ($\lambda = 0.710\,69$ Å) with an $\omega/2\theta$ scan technique. Lattice constants were determined by least-squares fitting of the setting angles of 1708 reflections for **1** and 25 for **2**–**6**. All intensities were corrected for Lorentz and polarization effects. The structures were solved by direct methods using the SIR92[21] system of programs and all other calculations were accomplished using SHELXL-97[22] and PARST.[23] All structures were refined on F^2 by full-matrix least-squares methods with anisotropic non-H atoms and isotropic hydrogens. Crystal data are reported in Table 2.

CCDC reference number 440/246. See http://www.rsc.org/suppdata/nj/b0/b008262g/ for crystallographic files in .cif format.

Acknowledgements

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