A structural and spectroscopic investigation of the hydrochlorination of 4,4'-methylenedianiline[†]

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The hydrochlorination of 4,4'-methylenedianiline, NH₂C₆H₄CH₂C₆H₄NH₂ (MDA), in chlorobenzene to produce 4.4'-methylenedianiline dihydrochloride, $[H_3NC_6H_4CH_2C_6H_4NH_3]Cl_2$ (MDA·2HCl) is an important reaction for the production of isocyanates, which are used to manufacture polyurethanes. This reaction is examined here. MDA is moderately soluble in chlorobenzene, whereas MDA 2HCl is effectively insoluble. Controlled addition of anhydrous HCl to MDA in chlorobenzene led to the isolation of a solid whose stoichiometry is MDA·HCl. Crystals obtained from solutions of MDA HCl in methanol were found by X-ray analysis to consist of the basic hydrochloride salt, [MDAH₂][Cl]₂[MDA]₂H₂O, which is stabilised by complex hydrogen-bonding. The starting material MDA has an H-bonded structure in which the molecules are linked in a one-dimensional chain. Hydrogen-bonding is extensive in MDA-2HCl which contains ladders of $[H_3NC_6H_4CH_2C_6H_4NH_3]^{2+}$ dications stabilised by N-H···Cl linkages. Energy calculations on the crystalline systems allow an identification of the main factors in intermolecular cohesion; these are related to melting temperature and solubility data. Such improvements in understanding of solute-solute interactions are prerequisites for improving the atom economy of this important stage within the polyurethane manufacture process chain. The solid phase IR spectrum of MDA 2HCl is diagnostic, principally as a result of a Fermi resonance process.

1. Introduction

Methylene diphenyl diisocyanate (MDI) and toluene diisocyanate (TDI) are the major isocyanates used to make polyurethanes,¹ having respective shares of the global isocyanate production of 60 and 34%.¹ Flexible foams used in household products such as furniture and mattresses are made mainly from TDI,² whereas foams of higher mechanical strength are typically made from symmetrical isocyanates such as MDI.³ The primary precursor for MDI is 4,4'-methylenedianiline (MDA),⁴ for which the total global production capacity in 2010 will be about 5 million tonnes.

MDI can be manufactured on the industrial scale by the phosgenation of MDA in a solvent such as chlorobenzene. A complicating feature of the phosgenation process is that the hydrogen chloride liberated reacts with the MDA starting material to form unwelcome hydrochloride salts.⁵ These secondary reactions are outlined as part of Scheme 1.

There are two features of the scheme which largely determined the way in which the study to be described here was carried out. First, isolation of the postulated intermediate, methylenedianiline monohydrochloride, $[H_2NC_6H_4CH_2C_6H_4NH_3]Cl$ (MDA·HCl) (3) has, as far as we are aware, not been reported in the open literature previously, although the properties of the compound are of potential interest in any modelling studies carried out on the large-scale phosgenation process. As will be described below, the reaction and product characteristics are consistent with two sequential hydrochlorination processes. Secondly, the reaction of MDA·HCl (3) with adventitious water present during attempted recrystallisation of the compound led unexpectedly to the isolation of a hydrate, which we formulate as a basic hydrochloride salt (4).

Because the hydrochloride salts, MDA·HCl and MDA· 2HCl, are effectively insoluble in the phosgenation process solvent, chlorobenzene, the study of their formation presents a considerable challenge. We have adopted an approach in which attention is directed to understanding those features of the solids from which useful information about the reactions in Scheme 1 can be inferred. The approach used is identical to that developed to study the hydrochlorination of the simple aromatic amine, 4-benzylaniline, 4-BA,⁶ and we examine here the formation and properties of hydrochloride salts originating from the industrially relevant MDA. The

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Scheme 1 Reaction of 4,4'-methylene dianiline (1) with HCl to form 4,4'-methylene dianiline monohydrochloride (3) and thence, 4,4'-methylene dianiline dihydrochloride (2). Recrystallisation of (3) to give a hydrate, formulated as a basic hydrochloride salt (4).

presence of two -NH₂ functional groups in MDA leads to complexities that were not found in the 4-BA/HCl/C₆H₅Cl system.⁶ The synthesis of the thermodynamically stable dihydrochloride, MDA 2HCl, is described and the procedure is modified for preparation of the monohydrochloride, MDA·HCl. Whereas a previous crystallographic study exists for the diamine,⁷ no such analysis apparently exists for the hydrochloride salts and data presented here show how hydrochlorination dramatically perturbs the structure of the parent molecule. These structures are compared with the rather complex hydrogen bonding arrangements found in the basic hydrochloride salt (4), which is the product of attempted recrystallisation of MDA·HCl from methanol containing adventitious water (Scheme 1). The forces acting between molecules in the crystals of MDA (1) and MDA·2HCl (2) were calculated by the PIXEL method.^{8,9} The relative magnitudes of these forces provide a valuable insight into the factors which influence solubility and hence mass transport criteria in chlorobenzene. Such improvements in understanding of solute-solute interactions are prerequisites for improving the atom economy of this important stage within the polyurethane manufacture process chain.

2. Experimental

2.1 Preparation of hydrochloride salts, MDA·2HCl (2) and MDA·HCl (3)

Chlorobenzene (Sigma-Aldrich, purity 99.8%, <0.005% water) was purified as described previously.⁶ Anhydrous HCl (anhydrous commercial grade, Linde Gas) was dispensed from a lecture bottle which was fitted with a regulator compatible with corrosive gases (Praxair, inlet pressure range 0–2.8 \times 10⁴ MPa, outlet range 0-700 MPa) and a stainless steel bonnet needle valve (Whitey) in order to control the gas flow into vacuum or flow apparatus. 4,4'-Methylene dianiline (Sigma-Aldrich, purity 97%, mp = 362-364 K, literature $mp = 375 \text{ K}^{10}$) was used without further purification. Melting points (uncorrected) were determined using a Stuart Scientific SMP1 instrument. Elemental analyses were obtained using a CE 440 Elemental Analyser (Exeter Analytical Inc.). The same procedure and glass reactor/gas manifold unit used to prepare 4-benzylaniline hydrochloride⁶ were used to prepare 4,4'-methylenedianiline dihydrochloride, MDA·2HCl (2). A colourless solid, mp = 534 K, precipitated from solution. Found C, 57.7; H, 5.9; Cl, 26.2; N, 10.2%. C₁₃H₁₆Cl₂N₂ req. C, 57.6; H, 5.9; Cl, 26.2; N, 10.3%. Modifications to the apparatus and procedure were necessary for the preparation of 4,4'methylenedianiline monohydrochloride, MDA HCl (3). Specifically, a detachable Pyrex cell was charged with a stoichiometric amount of HCl on a separate vacuum manifold. The HCl was then isolated and frozen using an isopentane/liquid nitrogen slush bath prior to re-connection to the flow apparatus. Controlled and gradual addition of the HCl within a nitrogen carrier gas feedstream to a degassed, vigorously stirred solution of MDA in chlorobenzene at 293 K afforded the reproducible preparation of MDA·HCl (3) as a colourless solid. Found (results from two different samples) C, 66.7, 66.6; H, 6.5, 6.4; Cl, 15.3, 15.2; N, 11.9, 11.8%. C₁₃H₁₅ClN₂ req. C, 66.5; H, 6.4; Cl, 15.1; N, 11.9%. Although a 1 : 1 mole ratio MDA : HCl was indicated by these analyses, the mp of the solid occurred over the range 461-498 K. It is possible that there is a slow loss of HCl when the material is heated.

2.2 Characterisation

Infrared spectra of the solids MDA (1), MDA-2HCl (2) and MDA·HCl (3) were obtained using ATR-FTIR spectroscopy (Pike MIRacle ATR accessory with diamond/ZnSe element used within a purged Nicolet Avatar 360 FTIR spectrometer). ¹H NMR spectra were obtained on solutions of the reagent and products using a Bruker Avance 400 MHz spectrometer. Frequency positions are quoted using the δ scale, with $\delta = 0$ referenced to TMS. The solutions were prepared by dissolving a few mg of sample in dimethyl sulfoxide-d₆ (Aldrich, 99.9 atom% D, < 50 ppm water). The ¹H NMR spectra of (1), (2), (3) and (4) in d_6 -DMSO were studied in order to provide chemical shift information for reasonably concentrated solutions. The spectra were characterised by chemical shifts for the $-NH_x$ (x = 2 or 3) species at $\delta = 4.8, 9.3, 7.9$ and 8.2 ppm respectively. In all cases the aromatic ring ¹H signals correspond to $[AA'BB']_2$ spin systems. The δ values for the CH₂ signals occurred at δ = 3.56, 3.92, 3.77 and 3.78 ppm respectively.

Solubility measurements in chlorobenzene were performed using ¹H NMR spectroscopy in a comparable fashion to that described in the 4-benzylaniline work,⁶ which had afforded a detection limit for 4-benzylaniline of 1×10^{-2} mmol dm⁻³. The concentration of solvated MDA (MDA_(solv)) was determined by integration of the CH₂ signal with reference to an internal standard, CH₂Cl₂.

Single crystals of MDA (1) were obtained from chlorobenzene. The solid MDA·2HCl (2) was recrystallised from methanol (AR grade, purity \geq 99.8%) in an atmosphere of chlorobenzene using a vapour-diffusion crystallisation procedure. Single crystals of both compounds were mounted on glass rods and transferred to the cold-gas stream of a Nonius Kappa CCD X-ray diffractometer for measurement. The structures were analysed using the WinGX and SHELX-97 software (see Table 1).^{11–13} The X-ray structural analysis on the sample obtained by recrystallising MDA·HCl (3) from MeOH established that a chemical change had occurred and that the composition of the crystal was in fact $[MDAH_2][Cl]_2[MDA]_2H_2O$ (4), *i.e.* $C_{39}H_{46}Cl_2N_6O$, which requires C, 68.3; H, 6.8; Cl, 10.3; N, 12.3; O, 2.3% and is thus incompatible with the analytical data obtained for (3) before recrystallisation (see above).

Standard refinement methods were used in the analyses. Thus, H atoms bonded to N or O atoms were freely refined, except for (**2**) where restraining the N–H distances to 0.86(2) Å slightly improved the results; the riding model was used throughout for C-bonded H atoms. For (**1**) dispersion is insignificant; accordingly, Friedel pairs were merged and the absolute structure was not determined. This contrasts with (**4**) where 2291 Friedel pairs were retained as separate observations and the Flack parameter of 0.01(4) indicates unambiguous determination of absolute structure.

2.3 Computational studies

Intermolecular energies were calculated for the crystal structures by the PIXEL method,^{8,9} or by the atom-atom potential energy method. The former method is based on

Table 1 Crystal data and structure refinements for compounds (1), (2) and $(4)^a$

	MDA (1)	MDA·2HCl (2)	[MDAH ₂][Cl] ₂ [MDA] ₂ H ₂ O (4	
Empirical formula	$C_{13}H_{14}N_2$	$C_{13}H_{16}Cl_2N_2$	C ₃₉ H ₄₆ Cl ₂ N ₆ O	
Formula weight	198.26	271.18	685.72	
Temperature/K	150	150	120	
Crystal system	Orthorhombic	Monoclinic	Monoclinic	
Space group	$P2_{1}2_{1}2_{1}$	P2/n	C2	
a/Å	5.9003(5)	6.0828(9)	25.6208(5)	
b/Å	9.5998(10)	4.5346(9)	5.7067(2)	
c/Å	19.1346(15)	24.586(5)	13.7826(5)	
$\dot{B}/^{\circ}$	()	90.694(12)	118.962(1)	
$V/Å^3$	1083.8(2)	678.1(2)	1763.1(1)	
Z	4	2	2	
No. measured	6216	7360	15 531	
No. unique, R_{int}	1427, 0.080	1194, 0.104	5192, 0.047	
No. observed $[I > 2\sigma(I)]$	924	776	4851	
Completeness (%) to θ_{max} (°)	97.4 to 27.5	98.0 to 25.1	98.6 to 30.5	
Data/parameters	1427/152	1194/90	5192/250	
$R_1, WR_2 [I > 2\sigma(I)]$	0.059, 0.098	0.071. 0.120	0.037, 0.082	
R_1 , w R_2 (all data)	0.114, 0.110	0.125, 0.136	0.042, 0.083	
$ \Delta \rho _{\rm max}/{\rm e} {\rm \AA}^{-3}$	0.18	0.45	0.30	
^a All measurements with Mo-Ka X-ra	ys, $\lambda = 0.71073$ Å. Full-matrix	least-squares refinement on F^2 .		

numerical integrations over molecular charge densities obtained by high-level, correlated quantum mechanical calculations, to obtain partitioned coulombic, polarization, dispersion and repulsion energy contributions. The atomatom calculations were carried out in the $E_{\rm UNI} + E_{\rm EHT}$ approximation, whereby total energies consist of a Buckingham-type 6-exp term and a coulombic term over atomic point charges calculated using a variant of the extended Huckel method (see also our previous work⁶ for more detail).

3. Results and discussion

3.1 Solubility measurements

The solubility of MDA (1) and MDA 2HCl (2) in chlorobenzene was investigated by ¹H NMR spectroscopy. The saturation concentration of MDA (1) in chlorobenzene at 298 K was found to be 0.138 ± 0.007 mol dm⁻³, with the error representing 1 standard deviation in 4 replicate measurements. This value is 34 times smaller than that of its monoamine analogue, 4-benzylaniline (4-BA),⁶ indicating that the extra amine group has a modestly detrimental effect on the solubilisation process. The salt, MDA·2HCl (2), was found to be insoluble in chlorobenzene at room temperature and even heating at 355 K for 5.8 h did not result in dissolution, as was shown by the absence of relevant signals in the ¹H NMR spectrum. Given that the spectral acquisition procedures selected afford a detection limit of 0.01 mmol dm⁻³ for 4-benzyl aniline,⁶ it is concluded that the solubility of MDA·2HCl (2) is less than 0.01 mmol dm^{-3} over this temperature range. Moreover, no amine signals were observed in the NMR spectrum, indicating that MDA 2HCl did not dissociate under these conditions to form MDA (or MDA HCl) in solution. The dissolution of MDA·HCl (3) was not investigated. Further, the solid present in these MDA 2HCl dissolution experiments was not checked to discover if any solution mediated phase transformation had taken place.

In contrast, 4-benzylaniline hydrochloride ($C_6H_5CH_2C_6H_4NH_2$ · HCl, 4BA·HCl) is sparingly soluble in chlorobenzene at ambient temperature (0.26 \pm 0.13 mmol dm⁻³). Thus, the significantly reduced solubility of MDA·2HCl (2) in chlorobenzene, even on warming to 355 K, indicates that the additional hydrochloride unit, known from the X-ray analysis to be ionic (see Section 3.2), significantly enhances the cohesive interactions within the solid, due to the strong coulombic component between ionic fragments, and thereby works against solubilisation by non-polar chlorobenzene molecules.

3.2 Crystal structure determinations

The structure of MDA (1) at room temperature has previously been reported; the slight differences between the results of Bel'skii *et al.*⁷ and those obtained by us at 150 K can be explained by the difference in temperature between the two experiments. A search of the Cambridge Structural Database, Version 5.30 of November 2008,^{14,15} for the *p*-N–(C₆H₄)–CH₂–(C₆H₄)–N-*p* fragment revealed a number of recent and relevant structural studies, either of salts of the $[p-H_3NC_6H_4CH_2C_6H_4NH_3-p]^{2+}$ dication¹⁶ or of the neutral $[p-H_2NC_6H_4CH_2C_6H_4NH_2-p]$ diamine co-crystallised with



Fig. 1 A view of the MDA (1) molecule. Here and in Fig. 3 and 5 30% probability ellipsoids are shown and phenyl rings are numbered cyclically Cn1–Cn6, with Cn1 bound to the central Cn methylene carbon atom and Cn4 attached to the amine nitrogen atom.

other species.¹⁷ There is a single report of a structure containing the monoprotonated diamine $[p-H_3NC_6H_4CH_2C_6H_4NH_2-p]^+$, Ph₂C(OH)CO₂⁻ being the counter-anion.¹⁸

3.2.1 Crystal structure of MDA (1). The crystal is built from discrete molecules (Fig. 1) in which the C12–C11–C1–C21–C22 sequence displays respective torsion angles of -17.8(5) and $-66.7(4)^{\circ}$ across the C1–C11 and C1–C21 bonds.

A search for intermolecular contacts using the WINGX version of PLATON¹² reveals three Cg $\cdot\cdot\cdot$ Cg distances < 5.5 Å, each of which is associated with a X-H···Cg interaction in which the H \cdots Cg distance is <3.1 Å, Table 2(a).‡ Furthermore, the molecules are linked into chains running parallel to the *c*-axis by moderate-to-weak¹⁹ $N \cdots H-N$ hydrogen bonds, Table 2(b) and Fig. 2. The significance of the contacts listed in Table 2(a) and (b) is best considered in the light of the lattice energy calculations reported in Section 3.3. However, it is worth pointing out here that (i) it is not obvious from Table 2(a) that the intermolecular interaction involving the C25-H25. Cg1ⁱ contact makes a larger contribution to the lattice energy than that which involves the N1-H111...Cg1ⁱⁱ contact and (ii) the search failed to find the second most important contributor to the lattice energy, namely the π - π interaction between the molecules related by translation along the short (5.90 Å) a-axis: the shortest intermolecular interatomic distance involving the operation 1 + x, y, z, that of 3.07 Å between H13...C16 is 0.17 Å greater than the sum of the H and C van der Waals radii.

3.2.2 Crystal structure of MDA·2HCl (2). The unit cell contains $[MDAH_2]^{2+}$ cations and chloride anions. Each cation (Fig. 3) has exact C_2 symmetry, with the diad passing through the methylene carbon atom C1, so that the two protonated aniline residues are related by the operation (i) 3/2 - x, y, 1/2 - z. The symmetrical conformation of the cation, defined by the C11ⁱ–C1–C11–C16 torsion angle of 71.7(5)°, contrasts with that of free MDA (1) (see Section 3.2.1).

Hydrogen bonding plays an important role, Table 2(c), in stabilising the crystal; each N–H bond of the cation donates a proton to a different Cl^- anion, so that at both ends of the MDA cation ribbons of H-bonds run parallel to the *a*-axis (Fig. 4). Similar ribbons of N–H···Cl bonds occur in 4-BA·HCl.⁶ The geometries of the three N–H···Cl bonds in MDA·2HCl (2) resemble both one another and those in aniline

[‡] Throughout this paper Cg is used to denote the centroid defined by the six carbon atoms of an aromatic ring.

Table 2 Geometry of intermolecular interactions (Å and $^{\circ}$) in MDA (1) and MDA·2HCl (2)^{*a,b,c*}

(a) $Cg \cdot \cdot \cdot Cg$ contacts	< 5.5 Å and as	sociated X−H····C	Cg contacts <3.1 Å in MDA (1)		
Contact	Distance	ϕ	$X\!\!-\!\!H\!\cdots\!Cg$	$Cg{\cdot}\cdot{\cdot}H$	${\scriptstyle \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	$Cg{\cdots} X$
$\begin{array}{c} Cg2\cdots Cg1^{i}\\ Cg1\cdots Cg1^{ii}\\ Cg1\cdots Cg2^{iii}\\ (b) Hydrogen bonds \end{array}$	5.03 5.22 5.38 in MDA (1)	58 47 86	C25-H25···Cg1 ⁱ N1-H111···Cg1 ⁱⁱ N1-H112···Cg2 ⁱⁱⁱ	3.03 2.89 2.73	139 166 141	3.80 3.77 3.55
A····H−D		d(H–D)	$d(\mathbf{A}\cdot\cdot\cdot\mathbf{H})$	$d(\mathbf{A}\cdot\cdot\cdot\mathbf{D})$		∠ A· · ·H–D
$N1 \cdots H221^{iv} - N2^{iv}$ (c) Hydrogen bonds	in MDA·2HCl	0.90(3) (2)	2.30(4)	3.172(5)		165(3)
D–H···A		d(D–H)	$d(\mathbf{H} \cdot \cdot \cdot \mathbf{A})$	<i>d</i> (D···A)	∠ D–H· · ·A
$\begin{array}{c} N1-H1N\cdots C11^{ii}\\ N1-H2N\cdots C11\\ N1-H3N\cdots C11^{iii} \end{array}$		0.87(2) 0.88(2) 0.87(2)	2.35(2) 2.25(2) 2.42(3)	3.190(5) 3.113(5) 3.233(5)		164(5) 165(5) 156(6)

^{*a*} Cg1 and Cg2 are the centroids of phenyl rings C11–C16 and C21–C26 and φ is the dihedral angle between phenyl rings in contact with one another. ^{*b*} Symmetry codes for MDA (1): (i) -x, 1/2 + y, 1/2 - z; (ii) -1/2 + x, 3/2 - y, 1 - z; (iii) 1/2 - x, 1 - y, 1/2 + z; (iv) -1/2 - x, 1 - y, 1/2 + z; (iv) -1/2 - x, 1 - y, 1/2 + z; (iv) -1/2 - x, 1 - y, 1/2 + z; (iv) -1/2 - x, 1 - y, 1/2 + z. ^{*c*} Symmetry codes for MDA·2HCl (2): (i) -x + 3/2, y, -z + 1/2; (ii) -x + 1, -y + 1, -z + 1; (iii) -x + 2, -y + 1, -z + 1.



Fig. 2 The MDA (1) unit cell viewed along the crystallographic *a*-axis. Chains of molecules running parallel to the horizontal *c*-axis are linked by $N-H\cdots N$ bonds.



Fig. 3 The MDA-2HCl (2) structure viewed down the diad axis passing through C1. See Table 2, footnote c for symmetry codes.

hydrochloride (N···Cl 3.16, 3.16 and 3.18 Å) which also contains $RNH_3^+Cl^-$ ion pairs.²⁰

Although the short *b*-axis of 4.53 Å might suggest that the $\pi-\pi$ interaction contributes significantly to the lattice energy, there are no particularly short individual interatomic contacts between cations related by translation along b; the shortest is the C1–H1…C16 distance of 2.94 Å.

3.2.3 Crystal structure determination of [MDAH₂][Cl]₂-[MDA]₂H₂O (4). As previously pointed out, recrystallisation of MDA·HCl (3) from methanol gave diffraction-quality crystals of a hydrated basic hydrochloride of formal composition 3MDA·2HCl,H₂O. The diffraction analysis establishes that



Fig. 4 The MDA·2HCl (2) unit cell viewed along the crystallographic *b*-axis, showing the ladder arrangement of $MDAH_2^{2+}$ cations arising from N–H···Cl H-bonding.

four distinct species are present and that the crystal is best represented by the formula $[MDAH_2][Cl]_2[MDA]_2H_2O$ (4). The diprotonated MDA cation and Cl⁻ counter-anion are shown, together with the MDA and water molecules in Fig. 5.

The methylene carbon atom of the $[MDAH_2]^{2+}$ cation, C21, and the water oxygen atom, O1, both lie on crystallographic diad axes. The conformation of the $[MDAH_2]^{2+}$ cation, defined by the C211¹–C21–C211–C216 torsion angle



Fig. 5 A view of the $[MDAH_2]^{2^+}$, [MDA], Cl^- and H_2O residues in (4). C21 and O1 lie on crystallographic C_2 axes. For symmetry codes see Table 4, footnote *a*.

of $38.0(1)^{\circ}$, is appreciably flatter than that in MDA·2HCl (2) where the corresponding angle is $71.7(5)^{\circ}$, while the torsion angles of $81.9(2)^{\circ}$ and $47.4(2)^{\circ}$ in the C116–C111–C11–C121–C126 chain of the neutral amine molecule compare with values of $-17.8(5)^{\circ}$ and $-66.7(4)^{\circ}$ in MDA (1). Evidently these torsion angles are largely determined by packing requirements.

The formation of (4) corresponds to the reaction between MDA·HCl (3) and water shown in eqn (1).

$$3MDA \cdot HCl_{(s)} + H_2O_{(l)} \rightarrow [MDA \cdot 2HCl + 2MDA + H_2O]_{(s)}$$
$$+ HCl_{(g)} \qquad (1)$$

It had been assumed that the compound would exist in methanol without change in stoichiometry (MDA·HCl) and that one amine group of the MDA molecule would be protonated. The methanol used was analytical reagent grade (purity $\geq 99.8\%$) but was not completely anhydrous. The

outcome is presumably a reflection of the importance of hydrogen bonding in the solid formed and is rationalised on the basis that water is a better H-bond acceptor than HCl. The HCl missing from the structure is believed to have been lost by evaporation with the methanol. As noted earlier, a salt of the monoprotonated diamine $[p-H_3NC_6H_4CH_2C_6H_4NH_2-p]^+$ presumed to be present in (3) has recently been structurally characterised.¹⁸

In crystals of (4) all four residues are involved in a complex network of hydrogen bonds (Fig. 6). In considering these, it is helpful to bear in mind the values of $H \cdots Cl$ distances that are regarded as typical for various types of $XH \cdots Cl$ hydrogen bond (Table 3). A $X-H \cdots Cl$ interaction has been included in the list of hydrogen bonds (Table 4) if the $H \cdots Cl$ distance is less than 3.0 Å, the sum of the van der Waals radii of H and Cl.

The $-NH_3^+$ nitrogen atom, N21, of the dipositively charged cation forms four hydrogen bonds: two to neutral amine nitrogen atoms N12ⁱ and N11 (bonds 4 and 6), one to C11^v (bond 7) and one to the water O1 atom (bond 5). Bonds 4 and 5 make up a bifurcated H-bond.²¹ Atoms N11 and N12 of the two neutral amine groups each form a N–H···Cl H-bond (bonds 1 and 2) in which the H···Cl distances, 2.48 and 2.59 Å, respectively, are long compared with the typical values of Table 3. In addition, N12 participates in a second and extremely weak interaction with Cl1^{iv} (bond 3, H···Cl = 2.85 Å). Furthermore, the free H1A donor atom bonded to

Table 3 Ranges of $H\!\cdots\!Cl$ distances in X–H $\cdots\!Cl$ hydrogen bonds according to Jeffrey 19

H-bond	H···Cl/Å			
	Min	Max		
$\overline{N^+(H_2)H\cdots Cl^-}$	2.12	2.15		
$N(H)H \cdot \cdot Cl^{-}$	2.14	2.35		
$O_w H \cdots Cl^-$	2.13	2.40		



Fig. 6 The structure of $[MDAH_2][Cl_2][MDA]_2H_2O$ (4) viewed in projection along the *b*-axis. In the projection plane *a* points upwards and *c* runs horizontally from right to left. Hydrogen bonds are indicated by the numbers defined in Table 4, except that the operation *x*, *y*, -1 + z has been applied to the bonds shown radiating from N12. Since N12 links chloride anions related by translation along *b*, bonds 2 and 3 appear to coincide in this view.

Table 4 Hydrogen bond parameters for $[MDAH_2][Cl]_2[MDA]_2H_2O$ (4) [Å and °]^{*a*}

No.	$D\!\!-\!\!H\!\!\cdot\!\cdot\!\cdot\!A$	<i>d</i> (D–H)	$d(H \cdots A)$	$d(\mathbf{D} \cdot \cdot \cdot \mathbf{A})$	∠(DHA)			
1	N11–H1B· · · Cl1 ⁱⁱ	0.91(2)	2.48(2)	3.388(1)	170(2)			
2	N12–H1C···Cl1 ⁱⁱⁱ	0.85(2)	2.59(2)	3.373(1)	153(2)			
3	N12–H1D· · · Cl1 ^{iv}	0.88(2)	2.85(2)	3.687(2)	158(2)			
4	$N21-H2A\cdots N12^{i}$	0.88(2)	2.19(2)	2.996(2)	154(2)			
5	N21–H2A···O1	0.88(2)	2.36(2)	2.803(2)	111(2)			
6	N21–H2B· · · N11	0.96(2)	1.94(2)	2.869(2)	161(2)			
7	N21–H2C···Cl1 ^v	0.90(2)	2.43(2)	3.196(1)	143(2)			
8	$O1-H1W\cdots Cl1^{ii}$	0.91(2)	2.21(2)	3.118(1)	177(2)			
^a Symmetry code: (i) $-x + 1$, $y, -z + 2$; (ii) $-x + 1/2$, $y - 1/2$, $-z + 1$;								
(iii) $-x + 1/2$, $y + 1/2$, $-z + 2$; (iv) $-x + 1/2$, $y - 1/2$, $-z + 2$;								
(v) -x + 1/2, y + 1/2, -z + 1.								

N11 is 3.05 Å from a Cl⁻ anion; this interaction is not listed in Table 4 as the H1A···Cl distance exceeds the sum of the van der Waals radii of H and Cl. A neutron diffraction study of bis(2-amino-2-methyl-3-butanone-oximato)nickel(II) chloride monohydrate²² reports NH···Cl⁻ bond lengths of 2.301 and 2.445 Å and bond angles of 161.9 and 174.0°, which can be compared to those found in [MDAH₂][Cl]₂[MDA]₂H₂O. As previously noted, the water oxygen, O1, accepts an H-bond from the N21 NH₃⁺ group but it also donates through H1W to Cl1ⁱⁱ (bond 8); the H···Cl distance of 2.21 Å is unexceptional (see Table 3).

The bifurcated H-bond²¹ found in the structure of $[MDAH_2][Cl]_2[MDA]_2H_2O$ (4) is common in proton deficient systems, such as amino acids, carbohydrates and esters. In a recent survey of 42 structures containing bifurcated bonds with ester O and amine N as acceptors, mean H···N and H···O distances of 2.31(6) and 2.44(10) Å, respectively, were found.²³ Comparing these values with H···N and H···O distances of 2.19(2) and 2.36(2) Å in the bifurcated system of (4) suggests bond 4 contributes more to the stability of (4) than bond 5. The acute N–H···O angle of 111° also indicates that bond 5 is relatively weak.

The hydrogen bonding scheme presented here for (4) makes use of all available donor H atoms, provided the very long $Cl \cdots NH_2$ contact of 3.05 Å is included, and also of all acceptor sites on N, O or Cl atoms. It gives rise to {MDAH₂, 2MDA} units with C_2 symmetry, two of which are shown in Fig. 6, each held together by four $NH_3^+ \rightarrow NH_2 N-H \cdots N$ hydrogen bonds. The structure is then completed through hydrogen bonding between this unit, water molecules and Cl^- anions. Although X–H $\rightarrow \pi$ -ring and π – π stacking interactions undoubtedly contribute to stabilising the crystal, they do not give rise to any anomalously short, inter-residue contacts.

It is well-known that monofunctional bases, B, such as aniline, form hydrochlorides B·HCl which are the chloride salts of the protonated base BH⁺. Less well known are the basic salts, B₂·HCl, which are also referred to as hemi-hydrochlorides, B· $^{1}_{2}$ HCl. Aniline, for example, is reported to form a hemihydrochloride but, surprisingly, the structure is not known.²⁴ Indeed, the only structurally characterised example of the hemihydrochloride of a simple primary amine appears to be that of cyclohexylamine; the structure contains equal numbers of neutral cyclohexylamine molecules and cyclohexylammonium chloride cation/anion pairs.²⁵ The present study shows that more complex possibilities can arise for bifunctional bases like MDA.

3.2.4 Other structural features. Protonation of an aromatic amine lengthens the Car-N bonds and systematically alters endocyclic C-C-C angles. Thus, database mean Car-X bond lengths are 1.394 and 1.465 Å for X=NH₂ and NH₃⁺, respectively;²⁶ corresponding mean values of 1.412(12) Å and 1.468(6) Å in (1), (2) and (4) (see Table 5) agree both with values of 1.421 and 1.462 Å from published MDA¹⁷ and $MDAH_2^{2+16}$ structures and with those of 1.416(5) and 1.458(4) Å in MDAH⁺.¹⁹ Likewise, the Cn2–Cn4–Cn6 endocyclic bond angle, where Cn4 is attached to the amine nitrogen, also changes systematically when the amine is protonated; the average value of this angle is $121.5(1)^{\circ}$ for the protonated amine rings in (2) and (4) and $118.4(7)^{\circ}$ for the unprotonated amine rings in (1) and (4); virtually identical values apply to published MDA structures.^{17,18} This change in bond angle can be attributed to the greater group electronegativity of NH3⁺ compared with NH2.²⁷ Variations in the angular geometry of monosubstituted benzene ring derivatives have been used as the basis of an approach to the estimation of group electronegativities.^{28–34} Thus, the acuteness of the mean C-Cn1-C angle of 117.8° for (1), (2) and (4) (Table 5) reflects electron release by the methylene group.

3.3 Intermolecular energies in MDA (1) and MDA·2HCl (2) crystals

Numerical results are summarised in Table 6, while structures are depicted in Fig. 7. For MDA, the hydrogen-bonded molecular pair has a higher coulombic-polarisation energy and a smaller dispersion contribution than other pairs. The presence of a hydrogen bond increases the coulombpolarization contribution to the lattice energy in the crystal

Table 5 Selected bond lengths and angles (Å and °) for MDA (1), MDA·2HCl (2) and [MDAH₂][Cl]₂[MDA]₂·H₂O (4)

Compound	MDA (1)		MDA·2HCl (2)	[MDAH ₂][Cl] ₂ [MDA] ₂ H ₂ O (4)			
Ring no. n C $n4$ -X, X =	$1 \over NH_2$	2 NH ₂	$\frac{1}{\mathrm{NH_3}^+}$	11 NH ₂	12 NH ₂	21 NH ₃ ⁺	
Cn4–N	1.409(4)	1.397(4)	1.472(6)	1.420(2)	1.423(2)	1.463(2)	
CH ₂ -C _{Ph}	1.523(4)	1.512(4)	1.511(6)	1.514(2)	1.521(2)	1.516(2)	
$\langle C - C \rangle_{Ph}$	1.388(2)	1.384(2)	1.380(7)	1.393(2)	1.394(2)	1.390(2)	
C-CH ₂ -C	115.6(2)		112.9(6)	115.7(2)		114.4(2)	
C-Cn1-C	117.2(2)	117.1(3)	117.4(5)	117.4(1)	117.7(1)	119.0(1)	
C–Cn4–C	118.4(2)	117.6(3)	121.6(5)	119.1(1)	118.8(1)	121.5(1)	

Table 6Molecule-molecule interaction energies in MDA (1) crystals.See Fig. 7 for the corresponding molecular structural diagrams

	PIXEL energies/kJ mol ⁻¹						
Molecular pair	E _{coul}	$E_{\rm pol}$	$E_{\rm disp}$	$E_{\rm rep}$	E _{tot}		
$C-H \rightarrow \pi \operatorname{ring}_{-x \ 1} + y \ 1 - z$	-12	-5	-31	18	-31		
$\pi_{-\pi}$ stacking $1 - r$ $\nu_{-\pi}$ z	-8	-2	-24	11	-23		
$\begin{array}{c} \text{H-bond} \\ 1 & \text{v} & 1 & \text{v} & 1 \neq 2 \end{array}$	-26	-9	-26	25	-22		
$n = \frac{1}{2} - x, \ 1 = y, \ \frac{1}{2} + 2$ $N = H \rightarrow \pi \text{ ring}$ $x = \frac{1}{2}, \ \frac{3}{2} - y, \ 1 = z$	-11	-5	-21	18	-19		



Fig. 7 Structural diagrams for the most relevant molecular-pair interactions in the crystal of MDA (1): C–H \rightarrow phenyl ring, π – π stacking, H-bond and N–H \rightarrow phenyl ring interactions. See Table 6 for the corresponding interaction energies.

of MDA with respect to the crystal of 4-benzylaniline (4-BA) $[E_{sub} = -108 \text{ kJ mol}^{-1}].^{6}$

The dihydrochloride salt, MDA·2HCl (2), contains one dipositively charged cation which is balanced by two chloride anions. The total sublimation energy is the sum of the packing energy of the ion triad as a whole, plus the energy of the interaction between the cation and the chloride anions within the triad. These energies are shown in Table 7. Given that the corresponding energy for 4-benzylaniline hydrochloride (4-BA·HCl) is -759 kJ mol⁻¹,⁶ it is clear that the values for MDA·2HCl (2) are close to twice the corresponding energies for 4-BA·HCl, as expected from the presence of two ionic sites instead of one.

The crystal structure of $[MDAH_2][Cl]_2[MDA]_2H_2O$ (4) contains four chemical residues: a doubly charged cation,

molecules of MDA and water, and chloride anions present in ratio 1 : 2 : 1 : 2. The present PIXEL implementation allows only up to two different chemical species in the same crystal, so a PIXEL calculation for (4) is impossible. However, using the atom-atom potential method (with atomic point charges calculated by the more accurate ESP procedure for the coulombic contribution) an approximation to the lattice energy was obtained for this complex species too (Table 7).

The heat of sublimation estimated by the atom-atom approach is nearly identical to the PIXEL values for MDA (1), and is broadly comparable to the PIXEL value for MDA·2HCl (2); the inclusion of penetration energies by PIXEL obviously provides a better estimate. Although the heat of sublimation calculated for (4) is only an approximation, it does show that the value lies between those of the free amine (1) and the hydrochloride (2).

The combination of information from single crystal X-ray diffraction and PIXEL calculations of crystal cohesion energies provides a pointer to the rationalization of the different solubilities of MDA (1) and MDA-2HCl (2) in chlorobenzene. The rationale follows that laid out in detail in our earlier study⁶ of 4-benzylaniline; the types of solid state interactions involved in the comparison between MDA and its hydrochloride salt are the same as those considered previously⁶ for the BA vs. BA HCl pair, although, as mentioned above, the energies involved now cover a wider range. Table 7 shows that the lattice energy of the dihydrochloride salt (2) is an order of magnitude larger than that of the free base, as expected for strong ionic bonds against the moderately polar, or largely dispersive, interactions in the uncharged species. The one dimensional H-bonding arrangement in MDA (1) crystals with its medium-strong binding energy is more prone to dissolution in chlorobenzene; on the other hand, in order to overcome the substantial stabilization of the solid, dissolution of MDA 2HCl (2) requires some combination of a large solvation enthalpy and a favourable entropy of solution, both conditions being unlikely to be met by a poor donor solvent like chlorobenzene. As described in Section 2.2, reagents and products (1), (2), (3) and (4) were all soluble in d_6 -DMSO, enabling ¹H NMR spectra to be recorded. Thus it is apparent that dissolution of MDA·2HCl is possible when a better donor solvent such as DMSO is used, which additionally has a greater permittivity.

3.4 FTIR spectroscopy

Infrared spectra in the 4000–2000 cm⁻¹ region for solid MDA (1) and MDA·2HCl (2) are shown in Fig. 8. Also shown are spectra for freshly-prepared MDA·HCl (3) and for [MDAH₂][Cl]₂[MDA]₂H₂O (4), obtained by recrystallisation

 Table 7
 Total lattice energies with PIXEL partitioning. The corresponding atom-atom estimates are also shown. Enthalpies of sublimation are approximated by the negative of the total lattice energies

		$E_{ m coul}/\ { m kJ\ mol}^{-1}$	$E_{ m pot}/\ { m kJ\ mol}^{-1}$	$E_{ m disp}/ m kJ\ mol^{-1}$	$E_{ m rep}/{ m kJ\ mol^{-1}}$	$E_{\rm tot} {\rm PIXEL}/{\rm kJ \ mol^{-1}}$	$\Delta E_{ m sub}/\ m kJ\ mol^{-1}$	$E_{\rm UNI + EHT}/kJ mol^{-1}$
MDA (1)		-74	-33	-134	110	-130	130	-127
MDA-2HCl (2)	Framework	-465	-176	-201	279	-562	1661	-1422
	Cation/Cl-	-1027	-160	-27	115	-1099		
[MDAH ₂][Cl] ₂ [MDA] ₂ H ₂ O (4)	,		_					-1331



Fig. 8 Reflectance FTIR spectra of solid compounds (1), (2), (3) and (4), shown in parts (a) to (d), respectively, in the region $4000-2000 \text{ cm}^{-1}$.

of (3) and characterised by X-ray analysis. A full vibrational analysis of MDA (1) and MDA·2HCl (2), involving infrared measurements, periodic DFT calculations and inelastic neutron scattering experiments and including some on selectively deuterated molecules, will be published elsewhere.³⁵

In a similar fashion to that observed for the 4-benzylaniline system,⁶ the N–H stretching region is highly diagnostic for discrimination between free amine and the hydrochloride salts.

Fig. 8(a) shows MDA (1) to be characterised by three bands at 3472, 3435 and 3329 cm⁻¹, attributed to anti-symmetric and symmetric stretches of the NH₂ group.³⁶ On hydrochlorination to MDA·2HCl (2), Fig. 8(b), these bands disappear and are replaced by broad bands in the region $3240-2610 \text{ cm}^{-1}$. In addition, an intense band about 2550 cm⁻¹ can be resolved into two features at 2574 and 2549 cm⁻¹. Following the approach presented in our earlier study,⁶ these two features about 2550 cm⁻¹ are assigned to Fermi resonance processes corresponding to combination bands of NH₃⁺ deformation modes and NH₃⁺ rocking modes. Specifically, the features arise from (i) a combination band comprising the antisymmetric NH₃⁺ deformation at 1498 cm⁻¹ and NH₃⁺ rock at 1061 cm^{-1} plus (ii) a combination band comprising the symmetric NH_3^+ deformation at 1437 cm⁻¹ and a NH_3^+ rock at 1118 cm⁻¹.

The intermediate compound, MDA·HCl (3), depicted in Fig. 8(c) displays intermediate behaviour between that of MDA (1) and MDA·2HCl (2). The NH₂ stretching modes are observed *ca*. 3300 cm⁻¹ in addition to the shifted N–H stretches of the NH₃⁺ group *ca*. 2800 cm⁻¹. More distinctly, an intense band at 2600 cm⁻¹ is also apparent, corresponding to the NH₃⁺ derived, Fermi resonance process described above. The presence of free amine (NH₂ derived modes) and protonated amine (NH₃⁺ derived modes) is consistent with hydrochlorination of a single amine group of the diamine molecule. This implies that hydrochlorination of the diamine (1) occurs in a sequential manner, as described by Scheme 1, where careful addition of one equivalent of HCl to a well-mixed solution of diamine will yield the monohydrochloride

 $(NH_2C_6H_4CH_2C_6H_4NH_2 \cdot HCl)$ (3). Although the features in Fig. 8(c) could correspond to those from a 1 : 1 mole ratio mixture of (1) and (2), the single crystal XRD data (Section 3.2.3) from the MeOH recrystallised product (4) favour its formulation as a single product.

The infrared spectrum of the recrystallised monohydrochloride (4), the composition of which corresponds to [MDAH₂][Cl]₂[MDA]₂H₂O, as determined by XRD (Section 3.2.3), is shown in Fig. 8(d). This spectrum is comparable to that of MDA·HCl (3), Fig. 8(c), but the bands are considerably broadened. This is attributed to the additional hydrogen bonding interactions within the [MDAH₂][Cl]₂[MDA]₂H₂O (4) structure. Both the NH_2 and NH_3^+ units are affected. The ν (N–H) vibration of NH₂ is represented by a broad band about 3280 cm^{-1} ; the Fermi resonance about 2600 cm^{-1} is also broadened compared with the equivalent bands in (2) and (3). The difference in the spectral profiles between Fig. 8(c) and (d) confirms that the monoprotonated base, MDA·HCl (3), has changed on crystallisation; the spectral features in Fig. 8(d), although not definitive on their own, are consistent with the formulation [MDAH₂][Cl]₂[MDA]₂H₂O (4) derived from the XRD analysis.

4. Conclusions

A variety of methods has been used in this study to examine some of the factors relevant to the hydrochlorination of 4,4'methylenedianiline, MDA, to form 4,4'-methylenedianiline dihydrochloride, MDA·2HCl, in chlorobenzene. The main results can be summarised as follows:

(i) 4,4'-Methylenedianiline dihydrochloride can be prepared from the reaction of solvated HCl and 4,4'-methylenedianiline in chlorobenzene. ¹H NMR spectroscopy showed the saturation concentration of MDA in chlorobenzene at 298 K to be 0.138 \pm 0.007 mol dm⁻³, whereas MDA·2HCl was effectively insoluble (<0.01 mmol dm⁻³) in this solvent. These values are considerably smaller than those for the analogous compounds containing one amino group.

(ii) 4,4'-Methylenedianiline monohydrochloride, MDA·HCl, can be prepared by controlled addition of HCl to MDA in the same solvent.

(iii) A detailed structural analysis of MDA and MDA 2HCl shows moderate-to-weak N-H···N hydrogen bonding in MDA while in the dihydrochloride each N-H bond donates a proton to a different Cl⁻ anion, resulting in ribbons of hydrogen bonds at both ends of the $[MDAH_2]^{2+}$ cations and the production of a coordination framework. Lattice energy calculations partitioned into coulombic and dispersive factors provide a rationalisation of the favourable interactions that contribute to stabilising the crystal structure of the neutral species and hydrochloride salt in the methylene diphenyl diisocyanate (MDI) process solvent, chlorobenzene. The greater lattice energy of the dihydrochloride salt ($E_{\text{lattice}} =$ $-1661 \text{ kJ mol}^{-1}$) compared with that of the free base $(E_{\text{lattice}} = -130 \text{ kJ mol}^{-1})$ provides a partial rationalisation of the solubility differences of the two compounds in chlorobenzene.

(iv) X-Ray analysis of crystals obtained from a solution of MDA·HCl in methanol indicates a composition

[MDAH₂][Cl]₂[MDA]₂H₂O resulting from displacement of HCl by water. H-bonding is extensive, with eight distinct H-bonds within the unit cell.

(v) As a collateral result, we confirm that intermolecular energy estimates, conveniently calculated between molecular pairs by PIXEL, allow a distinctly more accurate description and rationalization of crystal structures than is possible by traditional methods based on detailed consideration of interatomic distances and angles. It is often the case in organic crystals that relevant interactions are not characterised by short atom–atom distances, and *vice versa.*⁹

(vi) The infrared spectrum for the monohydrochloride, MDA·HCl, is consistent with the hydrochlorination of a single amine group leading to $[NH_2C_6H_4CH_2C_6H_4NH_3^+]Cl^-$, implying that hydrochlorination of the diamine is a sequential process.

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Notes and references

- 1 Y. Yakabe, K. M. Henderson, W. C Thompson, D. Pemberton, B. Tury and R. E. Bailey, *Environ. Sci. Technol.*, 1999, **33**, 2579–2583.
- 2 A. Marand, D. Karlsson, M. Dalene and G. Skarping, *Anal. Chim. Acta*, 2004, **510**, 109–119.
- 3 S. Subramani, I. W. Cheong and J. H. Kim, Prog. Org. Coat., 2004, 51, 328–338.
- 4 A. Corma, P. Botella and C. Mitchell, *Chem. Commun.*, 2004, 2008–2010.
- 5 D. Randall and S. Lee, *The Polyurethanes Book*, John Wiley & Sons, New York, 2002, p. 77.
- 6 E. K. Gibson, J. M. Winfield, K. W. Muir, R. H. Carr, A. Eaglesham, A. Gavezzotti, S. F. Parker and D. Lennon, *Phys. Chem. Chem. Phys.*, 2009, **11**, 288–297.
- 7 V. K. Bel'skii, V. K. Rotaru and M. M. Kruchinin, *Crystallogr. Rep.*, 1983, 28, 695–698.
- 8 A. Gavezzotti, J. Phys. Chem. B, 2003, 107, 2344-2353.
- 9 A. Gavezzotti, *Molecular Aggregation*, Oxford University Press, Oxford, 2007, ch. 12.
- 10 D. R. Lide, CRC Handbook of Chemistry and Physics, Taylor and Francis, London, 86th edn, 2005, pp. 3–221.
- 11 G. M. Sheldrick, SHELX97-Programs for Crystal Structure Analysis, 1998, (Release 97-2).
- 12 L. J. Farrugia, J. Appl. Crystallogr., 1999, 32, 837.

- 13 Z. Otwinowski and W. Minor, *Macromol. Crystallogr.*, 1997, 276, 307–326.
- 14 F. H. Allen, Acta Crystallogr., Sect. B: Struct. Sci., 2002, 58, 380–388.
- 15 D. A. Fletcher, R. F. McMeeking and D. Parkin, J. Chem. Inf. Comput. Sci., 1996, 36, 746–749.
- 16 (a) R. Nahouane, E. H. Soumhi, I. Saadoune and A. Driss, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2005, 61, 2850–2852;
 (b) L.-H. Wei, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2008, 64, 734; (c) Q. Han, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2007, 63, 4456; (d) Z.-L. Wang, L.-H. Wei, M.-X. Li and J.-P. Wang, J. Mol. Struct., 2008, 879, 150–155.
- (a) J. Keegan, P. E. Kruger, M. Nieuwenhuyzen, J. O'Brien and N. Martin, *Chem. Commun.*, 2001, 2192–2193; (b) A. J. Jarvis and P. G. Owston, J. Chem. Soc. D, 1971, 1403; (c) W. Swardstrom, D. P. Miller and L. A. Duvall, *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.*, 1972, 28, 2510–2514; (d) V. R. Vangala, R. Mondal, C. K. Broder, J. A. K. Howard and G. R. Desiraju, *Cryst. Growth Des.*, 2005, 5, 99–104.
- 18 J. Li, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2005, 61, 2850.
- 19 G. A. Jeffrey, An Introduction to Hydrogen Bonding, Oxford University Press, Oxford, 1997, pp. 12, 77.
- 20 J. F. Malone, C. M. Murray, M. H. Charlton, R. Docherty and A. J. Lavery, J. Chem. Soc., Faraday Trans., 1997, 93, 3429–3436.
- 21 G. A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer-Verlag, Berlin, 1991.
- 22 E. O. Schlemper, W. C. Hamilton and S. J. La Placa, J. Chem. Phys., 1971, 54, 3990–4000.
- 23 K. Molcanov, B. Kojić-Prodić and N. Raos, Acta Crystallogr., Sect. B: Struct. Sci., 2004, 60, 424–432.
- 24 J. C. Speakman, Struct. Bonding, 1972, 12, 141-199.
- 25 P. G. Jones and B. Ahrens, Eur. J. Org. Chem., 1998, 1687-1688.
- 26 C. H. MacGillavry and G. D. Rieck, *International Tables for X-ray Crystallography, Physical and Chemical Tables*, Kluwer Academic Publishers, Dordrecht, The Netherlands, 2nd edn, 1999, vol. C, I.U.Cr, Table 9.5.1.1.
- 27 A. Domenicano, A. Vaciago and C. Coulson, Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem., 1975, 31, 1630–1641.
- 28 A. R. Campanelli, A. Domenicano, F. Ramondo and I. Hargittai, J. Phys. Chem. A, 2004, 108, 4940.
- 29 H. Szatyłowicz and T. M. Krygowski, J. Mol. Struct., 2007, 844–845, 200–207.
- 30 G. Portalone, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2005, 61, 3083–3085.
- 31 G. Ploug-Sørensen and E. K. Andersen, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., 1985, C41, 613–615.
- 32 L. Gray and P. G. Jones, Z. Naturforsch., 2002, 57b, 61-72.
- 33 M. Colapietro, A. Domenicano, C. Marciante and G. Portalone, Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem., 1981, 37, 387–394.
- 34 A. Dey, R. K. R. Jetti, R. Boese and G. R. Desiraju, *CrystEngComm*, 2003, 5, 248–252.
- 35 E. K. Gibson, J. Callison, A. Sutherland, J. M. Winfield, R. Carr, A. Eaglesham, S. F. Parker and D. Lennon, to be submitted.
- 36 D. Lin-Vien, N. B. Colthup, W. G. Fateley and J. G. Grasselli, *The Handbook of Infrared and Raman Characteristic Frequencies of Organic Molecules*, Academic Press, London, 1991.