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Supramolecular structures in *N*-isonicotinoyl arylaldehydehydrazones: multiple hydrogen-bonding modes in series of geometric isomers

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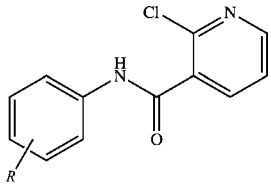
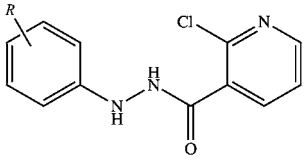
Sixteen *N*-isonicotinoyl arylaldehydehydrazones, $NC_5H_4CONHN{=}CHC_6H_4R$, have been studied and the structures of 14 of them have been determined, including the unsubstituted parent compound with R = H, and the complete sets of 2-, 3- and 4-substituted geometric isomers for R = F, Br and OMe, and two of the three isomers for R = Cl and OEt. The 2-chloro and 3-chloro derivatives are isostructural with the corresponding bromo isomers, and all compounds contain *trans* amide groups apart from the isostructural pair where R = 2-Cl and 2-Br, which contain *cis* amide groups. The structures exhibit a wide range of direction-specific intermolecular interactions, including eight types of hydrogen bonds, N—H···N, N—H···O, O—H···O, O—H···N, C—H···N, C—H···O, C—H···π(arene) and C—H···π(pyridyl), as well as π···π stacking interactions. The structures exhibit a very broad range of combinations of these interactions: the resulting hydrogen-bonded supramolecular structures range from one-dimensional when R = 2-F, 2-OMe or 2-OEt, *via* two-dimensional when R = 4-F, 3-Cl, 3-Br, 4-OMe or 3-OEt, to three-dimensional when R = H, 3-F, 2-Cl, 2-Br, 4-Br or 3-OMe. Minor changes in either the identity of the substituent or its location can lead to substantial changes in the pattern of supramolecular aggregation, posing significant problems of predictability. The new structures are compared with the recently published structures of the isomeric series having R = NO_2, with several monosubstituted analogues containing 2-pyridyl or 3-pyridyl units rather than 4-pyridyl, and with a number of examples having two or three substituents in the aryl ring: some 30 structures in all are discussed.

1. Introduction

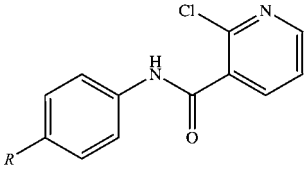
In recent years we have been very much interested in variations in crystal structures, as opposed to molecular structures, in various series of simple geometric isomers and, in particular, variations in the patterns of supramolecular aggregation determined by the direction-specific intermolecular forces (Cuffini *et al.*, 2006; de Souza *et al.*, 2005; Ferguson *et al.*, 2005; Glidewell *et al.*, 2002, 2006; Glidewell, Low, Skakle, Wardell & Wardell, 2005; Glidewell, Low, Skakle & Wardell, 2005; Kelly *et al.*, 2002; Wardell, Wardell *et al.*, 2002; Wardell, Low *et al.*, 2006; Wardell, de Souza *et al.*, 2007). As part of this general study, we have recently reported the supramolecular structures of the series of isomeric 1-(2-chloronicotinoyl)-2-nitrobenzamides (*A*, Scheme 1; de Souza *et al.*, 2005) and 1-(2-chloronicotinoyl)-2-(nitrophenyl)hydrazines (*B*; Wardell, de Souza, Wardell *et al.*, 2007), and of the series of 4-substituted *N*-aryl-2-chloronicotinamides (*C*; Cuffini *et al.*, 2006).



(*A*) *R* = 2-NO_2, 3-NO_2, 4-NO_2



(*B*) *R* = 2-NO_2, 3-NO_2, 4-NO_2



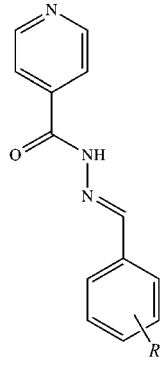
(*C*) *R* = H, Me, F, Cl, Br, I, OMe, CN

Scheme 1

In the benzamide series (*A*), the molecules of the 2-nitro isomer are linked by two independent C—H···O hydrogen bonds, one each with a carbonyl and a nitro O acceptor, into chains of edge-fused $R_2^2(14)$ and $R_4^4(24)$ rings, while in the 3-nitro isomer, which crystallizes as a monohydrate, a combination of N—H···O(water), O—H···O(carbonyl) and O—H···N (but not C—H···O) hydrogen bonds links the molecular components into chains of edge-fused rings containing two types of $R_4^4(16)$ ring. The 4-nitro isomer crystallizes with $Z' = 2$, and two independent N—H···N hydrogen bonds link the molecules into simple $C_2^2(12)$ chains (de Souza *et al.*, 2005).

The corresponding series of hydrazines (*B*), by contrast, shows more complex behaviour, not least because the 2-nitro isomer can be crystallized from different solvents in three polymorphic forms, although all of the crystalline forms are solvent free. Of the two monoclinic polymorphs of the 2-nitro isomer, the molecules in the *Cc* form are linked into sheets by one N—H···O(carbonyl) and two C—H···O(nitro) hydrogen bonds, while in the $P2_1$ form sheets are formed by the combined action of N—H···O(carbonyl), C—H···N and C—H···O(nitro) hydrogen bonds: in the orthorhombic (*Pbcn*) polymorph of this isomer, the molecules are linked into a complex three-dimensional framework by a combination of one N—H···O(nitro), one N—H···N and three C—H···O hydrogen bonds (one with a carbonyl acceptor and two with nitro acceptors), augmented by an aromatic $\pi\cdots\pi$ stacking interaction. A combination of N—H···O(carbonyl), N—H···N and C—H···O(nitro) hydrogen bonds links the molecules of the 3-nitro isomer into a three-dimensional framework, while a combination of N—H···O(carbonyl), N—H···N and C—H···O(carbonyl) hydrogen bonds links the molecules of the 4-nitro isomer into sheets (Wardell, de Souza *et al.*, 2007).

As an alternative to positional isomerism, structural diversity can also be introduced to a common skeletal framework *via* the variation of a single substituent at a fixed location, as in series (*C*) (Cuffini *et al.*, 2006). Each compound in this series exhibits only a modest number of direction-specific interactions, but the series as a whole manifests hydrogen bonds of N—H···O, N—H···N, C—H···O, C—H···N, C—H···π(arene) and C—H···π(pyridyl) types, as well as O—H···O and O—H···N types in the 4-fluoro derivative, which crystallizes as a monohydrate, together with a dipolar iodo···N(pyridyl) interaction in the 4-iodo compound and aromatic $\pi\cdots\pi$ stacking interactions in the 4-fluoro and 4-cyano derivatives. Overall, the resulting supramolecular structures span one-, two- and three-dimensional examples, but with no two compounds utilizing the same combination of direction-specific intermolecular interactions. It may be noted here that, apart from the dipolar interaction in the 4-iodo compound, the only direct participation in the supramolecular aggregation by the substituent *R* arises in the 4-cyano compound, which crystallizes with $Z' = 2$ and where the N atoms in both cyano groups act as acceptors in N—H···N hydrogen bonds. Even the halogen-substituted subset of (*C*), having F, Cl, Br or I as the substituent, all crystallize in different space groups, giving markedly different supramolecular structures.



(I) *R* = H
(II) *R* = 2-F, (III) *R* = 3-F, (IV) *R* = 4-F
(V) *R* = 2-Cl, (VI) *R* = 3-Cl, (VII) *R* = 4-Cl
(VIII) *R* = 2-Br, (IX) *R* = 3-Br, (X) *R* = 4-Br
(XI) *R* = 2-OMe, (XII) *R* = 3-OMe, (XIII) *R* = 4-OMe
(XIV) *R* = 2-OEt, (XV) *R* = 3-OEt, (XVI) *R* = 4-OEt
(XVII) *R* = 2-NO_2, (XVIII) *R* = 3-NO_2, (XIX) *R* = 4-NO_2
(XX) *R* = 4-CN

Scheme 2

With these sources of structural variation in mind, we have now undertaken a more systematic study of a related series of compounds, the substituted *N*-isonicotinoyl arylaldehydehydrazones (I)–(XVI) (Scheme 2), where we have been able not only to study examples containing a range of simple *R* substituents but, for most of these substituents, a full set of three geometric isomers. In addition, we have recently reported on the structures of compounds (XVII)–(XX)

Table 1
Experimental details.

	(I), *R* = H	(II), *R* = 2-F	(III), *R* = 3-F	(IV), *R* = 4-F	(V), *R* = 2-Cl
Crystal data					
Chemical formula	$C_{13}H_{11}N_3O$	$C_{13}H_{10}FN_3O$	$C_{13}H_{10}FN_3O$	$C_{13}H_{10}FN_3O\cdot H_2O$	$C_{13}H_{10}ClN_3O$
M_r	225.25	243.24	243.24	261.26	259.69
Cell setting, space group	Orthorhombic, *Pbca*	Triclinic, $P\bar{1}$	Orthorhombic, *Pbca*	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1/c$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)	120 (2)
a, *b*, *c* (Å)	7.1927 (2), 21.2168 (7), 28.6771 (10)	7.4815 (2), 11.1344 (2), 14.5365 (3)	13.1910 (4), 18.8057 (6), 18.2843 (4)	6.4189 (3), 6.8520 (3), 27.3451 (12)	7.9977 (2), 6.7184 (2), 22.5514 (6)
α, β, γ (°)	90, 90, 90	90.663 (2), 104.903 (3), 109.268 (2)	90, 90, 90	90, 90, 90	90, 98.609 (3), 90
V (Å^3)	4376.3 (2)	1098.45 (5)	4535.7 (2)	1202.70 (9)	1198.07 (6)
Z	16	4	16	4	4
D_x (Mg m^{-3})	1.367	1.471	1.425	1.443	1.440
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.09	0.11	0.11	0.11	0.31
Crystal form, colour	Block, colourless	Needle, colourless	Needle, colourless	Block, colourless	Plate, colourless
Crystal size (mm)	0.50 × 0.25 × 0.20	0.36 × 0.04 × 0.02	0.12 × 0.06 × 0.04	0.48 × 0.38 × 0.22	0.40 × 0.14 × 0.02
Data collection					
Diffractometer	Bruker–Nonius KappaCCD	Bruker–Nonius KappaCCD	Bruker–Nonius KappaCCD	Bruker–Nonius KappaCCD	Bruker–Nonius KappaCCD
Data collection method	φ and ω scans	φ and ω scans	φ and ω scans	φ and ω scans	φ and ω scans
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.966	0.969	0.975	0.960	0.893
T_{max}	0.982	0.998	0.996	0.976	0.994
No. of measured, independent and observed reflections	24 117, 4964, 3331	24 858, 5044, 3443	32 649, 5207, 3977	8595, 1630, 1412	18 325, 2757, 2159
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.050	0.058	0.071	0.031	0.042
θ_{max} (°)	27.5	27.5	27.6	27.5	27.5
Refinement					
Refinement on	F^2	F^2	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.047, 0.133, 1.05	0.053, 0.125, 1.03	0.063, 0.151, 1.10	0.034, 0.088, 1.03	0.037, 0.098, 1.03
No. of reflections	4964	5044	5207	1630	2757
No. of parameters	308	325	336	176	163
H-atom treatment	Constrained to parent site	Constrained to parent site	Constrained to parent site	Constrained to parent site	Constrained to parent site
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0763P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0609P)^2 + 0.2769P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0684P)^2 + 1.9661P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.050P)^2 + 0.2601P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 0.4843P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.42, −0.48	0.23, −0.31	0.67, −0.66	0.21, −0.19	0.31, −0.29
Extinction method	*SHELXL*	None	*SHELXL*	None	None
Extinction coefficient	0.0051 (8)	–	0.0206 (14)	–	–
Absolute structure	–	–	–	Friedel pairs merged	–

	(VI), *R* = 3-Cl	(VIII), *R* = 2-Brl	(IX), *R* = 3-Br	(X), *R* = 4-Br	(XI), *R* = 2-OMe
Crystal data					
Chemical formula	$C_{13}H_{10}ClN_3O$	$C_{13}H_{10}BrN_3O$	$C_{13}H_{10}BrN_3O$	$C_{13}H_{10}BrN_3O\cdot H_2O$	$C_{14}H_{13}N_3O_2$
M_r	259.69	304.15	304.15	322.17	255.27
Cell setting, space group	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)	120 (2)
a, *b*, *c* (Å)	7.4524 (3), 11.2367 (4), 14.3949 (3)	8.0268 (2), 6.7134 (3), 22.5024 (10)	7.4578 (2), 11.3264 (3), 14.3558 (3)	14.2570 (3), 14.6299 (4), 14.1669 (4)	9.8899 (3), 15.8189 (4), 17.0380 (5)
β (°)	102.701 (2)	99.297 (3)	101.119 (2)	119.152 (2)	97.236 (2)
V (Å^3)	1175.94 (7)	1196.66 (8)	1189.87 (5)	2580.61 (12)	2644.32 (13)
Z	4	4	4	8	8
D_x (Mg m^{-3})	1.467	1.688	1.698	1.658	1.282
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.32	3.43	3.45	3.19	0.09
Crystal form, colour	Block, colourless	Lath, colourless	Plate, colourless	Block, colourless	Needle, colourless
Crystal size (mm)	0.34 × 0.28 × 0.18	0.12 × 0.03 × 0.02	0.40 × 0.20 × 0.02	0.38 × 0.24 × 0.24	0.40 × 0.08 × 0.05

Table 1 (continued)

	(VI), *R* = 3-Cl	(VIII), *R* = 2-BrI	(IX), *R* = 3-Br	(X), *R* = 4-Br	(XI), *R* = 2-OMe
Data collection					
Diffractometer	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD
Data collection method	φ and ω scans	φ and ω scans	φ and ω scans	φ and ω scans	φ and ω scans
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.886	0.654	0.340	0.341	0.974
T_{max}	0.946	0.935	0.934	0.465	0.996
No. of measured, independent and observed reflections	15 675, 2691, 2076	11 911, 2746, 2182	14 830, 2733, 2231	28 990, 5916, 5220	33 120, 6048, 4196
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.034	0.062	0.043	0.045	0.053
θ_{max} (°)	27.5	27.7	27.5	27.5	27.5
Refinement					
Refinement on	F^2	F^2	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.038, 0.143, 1.08	0.041, 0.093, 1.06	0.028, 0.073, 1.07	0.058, 0.157, 1.23	0.052, 0.106, 1.02
No. of reflections	2691	2746	2733	5916	6048
No. of parameters	163	163	164	344	345
H-atom treatment	Constrained to parent site	Constrained to parent site	Constrained to parent site	Constrained to parent site	Constrained to parent site
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0972P)^2 + 0.0157P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0225P)^2 + 1.7209P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0343P)^2 + 0.5661P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.017P)^2 + 24.843P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0411P)^2 + 0.7605P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.001	< 0.0001	0.002	< 0.0001	< 0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.38, −0.33	0.45, −0.58	0.41, −0.55	2.26, −0.73	0.19, −0.21
Extinction method	None	None	*SHELXL*	None	None
Extinction coefficient	–	–	0.0049 (8)	–	–

	(XII), *R* = 3-OMe	(XIII), *R* = 4-OMe	(XIV), *R* = 2-OEt	(XV), *R* = 3-OEt
Crystal data				
Chemical formula	$C_{14}H_{13}N_3O_2$	$C_{14}H_{13}N_3O_2{\cdot}H_2O$	$C_{15}H_{15}N_3O_2$	$C_{15}H_{15}N_3O_2$
M_r	255.27	273.29	269.30	269.30
Cell setting, space group	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)
a, b, c (Å)	8.2938 (4), 11.0771 (6), 13.846 (5)	7.2702 (2), 12.3085 (5), 14.7299 (6)	8.3787 (3), 18.2450 (7), 17.870 (7)	24.2060 (17), 5.5637 (4), 9.9571 (4)
β (°)	103.478 (3)	97.370 (3)	90.975 (2)	94.965 (4)
V (Å^3)	1237.0 (5)	1307.22 (8)	2731.40 (18)	1335.94 (14)
Z	4	4	8	4
D_x (Mg m^{-3})	1.371	1.389	1.310	1.339
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.10	0.10	0.09	0.09
Crystal form, colour	Plate, colourless	Plate, colourless	Block, colourless	Block, colourless
Crystal size (mm)	0.15 × 0.15 × 0.04	0.36 × 0.18 × 0.05	0.15 × 0.10 × 0.10	0.10 × 0.04 × 0.03
Data collection				
Diffractometer	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD	Bruker-Nonius KappaCCD
Data collection method	φ and ω scans	φ and ω scans	φ and ω scans	φ and ω scans
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.977	0.972	0.977	0.985
T_{max}	0.996	0.995	0.991	0.997
No. of measured, independent and observed reflections	14 906, 2827, 1776	14 720, 3002, 2550	36 314, 6259, 3252	17 209, 3089, 2245
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.058	0.054	0.101	0.077
θ_{max} (°)	27.5	27.6	27.5	27.9
Refinement				
Refinement on	F^2	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.047, 0.162, 1.09	0.057, 0.142, 1.07	0.056, 0.137, 1.00	0.069, 0.221, 1.09
No. of reflections	2827	3002	6259	3089
No. of parameters	173	182	363	182
H-atom treatment	Constrained to parent site	Constrained to parent site	Constrained to parent site	Constrained to parent site

Table 1 (continued)

	(XII), R = 3-OMe	(XIII), R = 4-OMe	(XIV), R = 2-OEt	(XV), R = 3-OEt
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0889P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0518P)^2 + 1.3161P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0646P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.1145P)^2 + 0.807P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.0001	< 0.0001	< 0.0001	0.001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.28, −0.33	0.55, −0.26	0.20, −0.22	0.32, −0.31
Extinction method	None	None	None	None

Computer programs used: *COLLECT* (Hooft, 1999), *DENZO* and *COLLECT* (Otwinowski & Minor, 1997), *OSCAIL* (McArdle, 2003), *SHELXS*97 (Sheldrick, 1997*a*), *SHELXL*97 (Sheldrick, 1997*b*), *PLATON* (Spek, 2003), *PRPKAPPA* (Ferguson, 1999).

(Wardell, de Souza *et al.*, 2006; de Souza *et al.*, 2007), permitting a comparison of sets of geometric isomers for a substantial variety of substituents.

2. Experimental

2.1. Syntheses

The synthesis of (I)–(XVI) followed a common general procedure. Isonicotinoylhydrazine (2 mmol) was dissolved in water (10 cm^3), and the appropriate benzaldehyde (2 mmol) was separately dissolved in ethanol (10 cm^3); these solutions were then mixed and the mixture was stirred at ambient temperature for 2–6 h; the solvent was removed under reduced pressure and the residue was washed successively with cold ethanol and cold diethyl ether to give the crude products. Crystallization was from ethanol for (I)–(VII), (XI), (XII), (XIV) and (XVI); from methanol for (IX); from 2-propanol for (VIII); from acetone for (X) and (XIII); and from chloroform/2-propanol (1/1 v/v) for (XV); (IV), (X) and (XIII) were subsequently found to have crystallized as stoichiometric monohydrates. Melting temperatures: (I) 444–445 K, (II) 464–465 K, (III) 453–454 K, (IV) 443–445 K, (V) 463–464 K, (VI) 470–471 K, (VII) 462–464 K, (VIII) 502–503 K, (IX) 481–482 K, (X) 469–470 K, (XI) 464–466 K, (XII) 462–463 K, (XIII) 414–415 K, (XIV) 425–427 K, (XV) 421–422 K and (XVI) 423–424 K.

2.2. Data collection, structure solution and refinement

Details of cell data, data collection and structure solution and refinement are summarized in Table 1 (Ferguson, 1999; Hooft, 1999; McArdle, 2003; Otwinowski & Minor, 1997; Sheldrick, 1997*a*,*b*, 2003; Spek, 2003). Unique assignments of space groups were made from the systematic absences for each of compounds (I), (III)–(VI) and (VIII)–(XV): crystals of (II) are triclinic and the space group $P\overline{1}$ was selected, and subsequently confirmed by structure analysis. In all cases where Z' = 2, searches for possible additional symmetry using the ADDSYM option in *PLATON* (Spek, 2003) revealed none; likewise, no additional symmetry was detected in (IV). The structures were all solved by direct methods using *SHELXS*97 (Sheldrick, 1997*a*), and refined on F^2 with all data using *SHELXL*97 (Sheldrick, 1997*b*). A weighting scheme based upon $P = [F_o^2 + 2F_c^2]/3$ was employed in order to reduce statistical bias (Wilson, 1976). All H atoms were located in difference maps and then treated as riding atoms; H atoms bonded to C atoms had distances of 0.95 Å and U_{iso}(H) = 1.2U_{eq}(C); H atoms bonded to N atoms were permitted to ride at the N—H distances deduced from the difference maps, 0.88–0.96 Å, and with U_{iso}(H) = 1.2U_{eq}(N); H atoms bonded to O atoms were permitted to ride at the O—H distances deduced from the difference maps, 0.84–1.00 Å, and with U_{iso}(H) = 1.5U_{eq}(O). It was apparent from an early stage in the refinement of (III) that in one of the molecules the 3-fluorophenyl ring was disordered by a rotation of 180° about the exocyclic C—C bond. This disorder was modelled by using two sets of sites for the atoms F43 and H45, giving final refined occupancy factors for the major and minor conformers of 0.652 (4) and 0.348 (4), respectively. For (IV), the Flack parameter (Flack, 1983) was indeterminate (Flack & Bernardinelli, 2000) because of the absence of significant resonant scattering; consequently, the Friedel-equivalent reflections were merged prior to the final refinements and it was thus not possible to determine the absolute configuration of the molecules in the crystal selected for data collection: however, this has no chemical significance.

Supramolecular analyses were made, and the diagrams were prepared with the aid of *PLATON* (Spek, 2003). Fig. 1 shows the independent components and conformations of representative compounds with the atom-labelling schemes, and Figs. 2–8 show aspects of the supramolecular structures. Selected torsional angles are given in Table 2 and details of the hydrogen bonding are in Table 3.[1]

3. Results and discussion

3.1. Crystallization characteristics

The 2-chlorophenyl and 3-chlorophenyl derivatives (V) and (VI) are isomorphous and isostructural with the bromophenyl analogues (VIII) and (IX), respectively. The 3-methoxy compound (XII) has cell dimensions which are somewhat similar to those of (VI) and (IX), and the corresponding atom coordinates also resemble those of (VI) and (IX). However, detailed comparison of the unit-cell dimensions indicates the following changes on going from (VI) to (IX) to (XII): the changes in the dimension are, in a, + 0.0054 (3) and +0.8360 (4) Å, in b, +0.0897 (4) and −0.2493 (6) Å, and in c −0.0391 (3) and −0.510 (5) Å, respectively, with corre-

[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM5048). Services for accessing these data are described at the back of the journal.

sponding changes in the unit-cell volume of +13.93 (7) and 47.1 (5) Å^3, respectively. On this basis, (XII) should not be regarded as isostructural with (VI) and (IX) (Bajue *et al.*, 2003). Moreover, the direction-specific intermolecular interactions (Table 3) are identical in (VI) and IX), but different for (XII), and the hydrogen-bonded aggregation in (VI) and (IX) is two-dimensional, whereas that in (XII) is three-dimensional. We have been unable to obtain suitable crystals of the 4-chloro compound (VII) for comparison with the 4-bromophenyl compound (X). Similarly we have been unable to crystallize the 4-ethoxyphenyl compound (XVI).

Each of the 4-substituted derivatives reported here, (IV), (X) and (XIII), crystallizes as a monohydrate, as does the 4-cyanophenyl compound (XXI) (de Souza *et al.*, 2007), whereas all the 2- and 3-substituted compounds, as well as the unsubstituted parent compound (I) crystallize in anhydrous, and

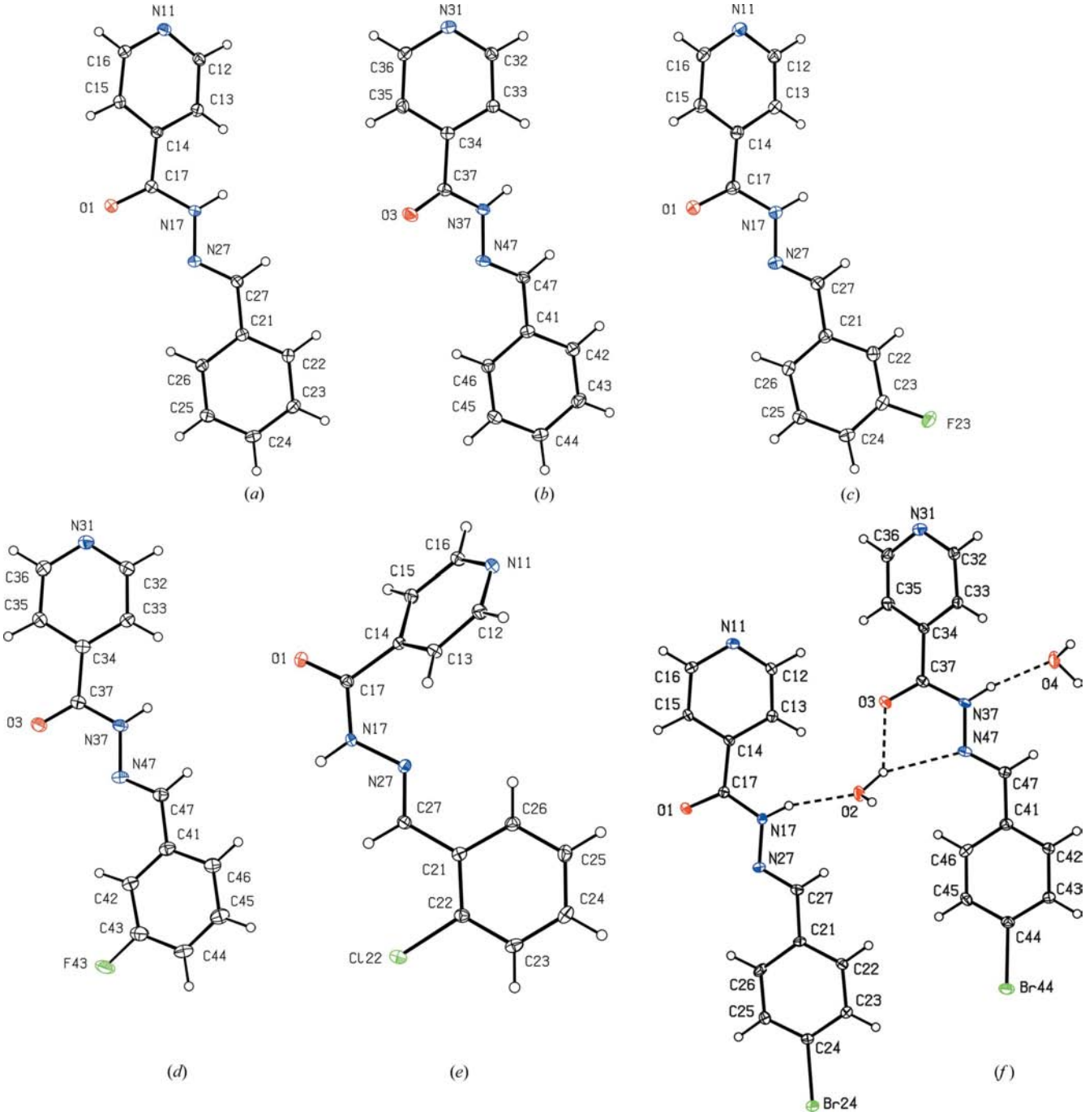


Figure 1
The molecular structures of representative compounds, with displacement ellipsoids drawn at the 30% probability level, selected to show the atom-labelling schemes and the different molecular conformations: (*a*) and (*b*) the two independent molecules of the unsubstituted compound (I); (*c*) molecule 1 of the 3-fluorophenyl compound (III); (*d*) the major orientation of molecule 2 of the 3-fluorophenyl compound (III); (*e*) the molecule of the 2-chlorophenyl compound (V); (*f*) the independent molecular components of the 4-bromophenyl compound (X).

indeed, solvent-free forms. We also note that the 3-nitrophenyl derivative has recently been reported both as the solvent-free form (XIII) (Wardell, de Souza, Wardell *et al.*, 2005) and as the monohydrate (XX) (Wardell, Wardell *et al.*, 2007). Compounds (I)–(III), (X), (XI) and (XIV) all crystallize with $Z' = 2$; for all these compounds we denote the molecules containing N11 and N31 as type 1 and type 2, respectively. While the majority of the compounds reported here crystallize in one of the common space groups ($P\bar{1}$, $P2_1/c$ and $P2_1/n$ or $Pbca$), the 4-fluorophenyl derivative (IV) and the 4-cyanophenyl derivative (XXI) (de Souza *et al.*, 2007) both unexpectedly crystallize in the Sohnke space group $P2_12_12_1$ so that these crystal structures are chiral even though their space group is achiral (Flack, 2003).

No polymorphic forms have been observed within this series, and no deliberate search for polymorphs has been undertaken.

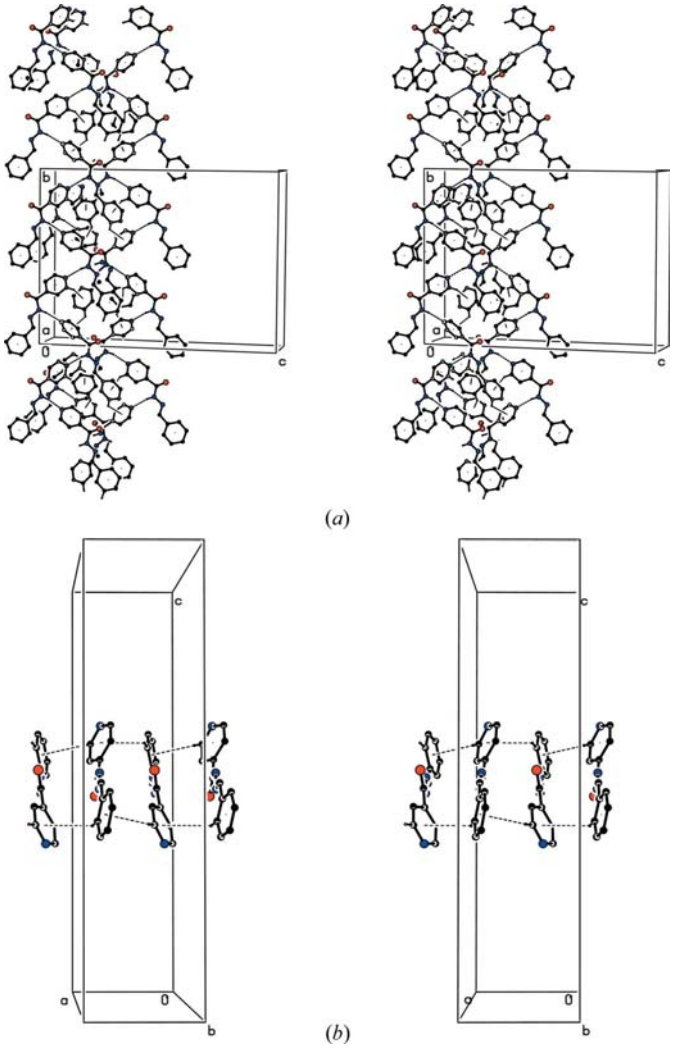


Figure 2
Stereoviews of parts of the crystal structure of (I) showing (*a*) the combination of the two motifs parallel to [010] forming a sheet parallel to (001), and (*b*) the ladder parallel to [100] which links adjacent (001) sheets. For the sake of clarity the H atoms not involved in the motifs shown have been omitted.

3.2. Previous determinations

A few of the structures discussed here have been reported before, always determined from diffraction data collected at ambient temperature. In each such case, the unit-cell parameters, space groups and the atomic coordinates indicate that the same phase was studied at ambient temperatures and 120 K. However, without exception, these previous reports provide extremely brief structure descriptions, with no analysis of the supramolecular aggregation. In a report on the 3-bromophenyl compound (IX), the authors stated that the structure 'is stabilized by intermolecular N—H···N hydrogen bonds' (Qiu, Fang *et al.* 2006), but the nature of the supramolecular structure was not further discussed. Similarly, in a report on the 2-methoxyphenyl derivative (XI), the authors stated only that the structure 'is stabilized by intermolecular N—H···O and N—H···N hydrogen bonds' (Yang *et al.*, 2006). There have been two previous reports on the hydrated 4-methoxyphenyl compound (XIII). The earlier of these (Shanmuga Sundara Raj *et al.*, 1999) stated only that 'the water and hydroxyl group are involved in a variety of N—H···O and O—H···N hydrogen bonds', even though no hydroxyl group is present; while the more recent report (Jing *et al.*, 2005), which did not mention the earlier one, identified O—H···O, O—H···N and N—H···O hydrogen bonds, all involving the water molecule, but did not analyse or describe the structural consequences of these hydrogen bonds. Whenever these reports provided a depiction of the crystal structure (Jing *et al.*, 2005; Qiu, Fang *et al.*, 2006; Yang *et al.*, 2006), neither the illustration itself nor the accompanying caption was really informative. In the course of the present study, we have now redetermined these structures from diffraction data

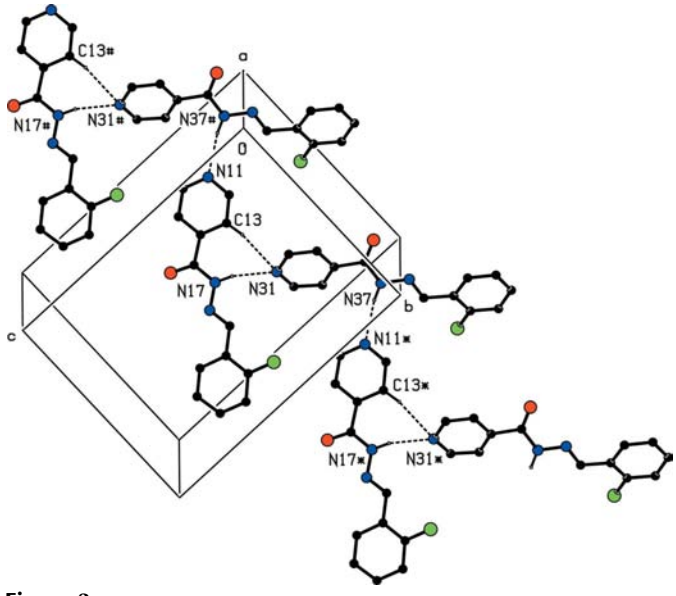


Figure 3
Part of the crystal structure of the 2-fluorophenyl compound (II) showing the formation of a chain of rings along [101]. For the sake of clarity the H atoms not involved in the motif shown have been omitted. The atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(x, 1 + y, z)$ and $(x, -1 + y, z)$, respectively.

Table 2
Selected torsional angles (°) (x = 1 or 3, y = 2 or 4).

Compound	Cx3—Cx4—Cx7—Nx7	Cx4—Cx7—Nx7—Ny7	Ny7—Cy7—Cy1—Cy2
(I)			
x = 1, y = 2	28.4 (2)	−176.49 (11)	164.93 (15)
x = 3, y = 4	−32.1 (2)	−178.82 (13)	−175.26 (15)
(II)			
x = 1, y = 2	7.4 (2)	−179.74 (13)	169.03 (16)
x = 3, y = 4	−24.9 (2)	178.37 (14)	−163.00 (16)
(III)			
x = 1, y = 2	23.8 (3)	174.52 (16)	177.60 (19)
x = 3, y = 4	9.3 (3)	−177.11 (16)	0.5 (3)
(IV)			
x = 1, y = 2	32.1 (3)	175.40 (15)	166.14 (18)
(V)			
x = 1, y = 2	−41.0 (2)	−12.9 (2)	−177.67 (14)
(VI)			
x = 1, y = 2	−5.0 (2)	177.67 (13)	2.6 (2)
(VIII)			
x = 1, y = 2	−41.0 (4)	−13.2 (4)	−177.6 (3)
(IX)			
x = 1, y = 2	−3.6 (3)	177.46 (15)	2.8 (3)
(X)			
x = 1, y = 2	24.2 (9)	176.2 (5)	177.9 (6)
x = 3, y = 4	−26.6 (9)	−179.9 (5)	−168.7 (6)
(XI)			
x = 1, y = 2	41.5 (2)	−179.96 (12)	176.53 (15)
x = 3, y = 4	−14.9 (2)	171.40 (12)	−177.80 (14)
(XII)			
x = 1, y = 2	−6.6 (3)	177.58 (16)	3.0 (3)
(XIII)			
x = 1, y = 2	38.9 (3)	171.75 (15)	175.35 (18)
(XIV)			
x = 1, y = 2	−33.7 (3)	−178.80 (15)	−171.40 (19)
x = 3, y = 4	15.6 (3)	−178.23 (15)	173.85 (19)
(XV)			
x = 1, y = 2	27.8 (4)	−179.9 (2)	−19.4 (4)

collected at 120 K and we provide here complete descriptions of the supramolecular structures for these compounds.

We also note here a report (Qiu, Xu *et al.*, 2006) on the dihydrated form of the 2-methoxyphenyl derivative (XI), which again stated only that 'the molecules are linked through weak intermolecular O—H···O and O—H···N hydrogen bonds'. The authors selected a non-connected asymmetric unit and provided a rather uninformative packing diagram in which the hydrogen bonds depicted do not appear to be consistent with those tabulated in the text. We shall return to this structure in §3.4.4.

3.3. Molecular conformations

The conformations of each molecular skeleton can be defined in terms of five torsional angles, three defining the conformation of the central spacer unit between the two rings and two defining the orientation of the rings themselves. Each compound has the (*E*) configuration at the C—N double bond within the spacer unit, and the N—N═C—C torsional angles deviate by no more than ±7° from 180°. Similarly the C—N—N═C torsional angles differ by no more than ±10° from 180°. The rotation of the rings out of the approximate plane of the spacer unit is sufficiently modest in every case to allow the clear identification of distinct edges to the rather elongated molecules. However, the remaining skeletal torsional angles (Table 2) show some unexpected variations. The angles Cx4—Cx7—Nx7—Ny7 (x, y = 1, 2 or 3, 4) are in general very close to 180°, corresponding to the usual *trans* amide linkage, but in the isostructural pair (V) and (VIII) this angle indicates the presence of *cis* amide linkages (Fig. 1*e*). At the same time, the 2-halogen substituent in each of the *cis* amides (V) and (VIII) is on the same edge of the molecule as the N—H bond, whereas in each of the isomeric *trans* amides (VI) and (IX), the 3-halogen substituent is on the edge opposite the N—H bond.

A somewhat similar phenomenon is apparent in the two independent molecules of the 3-fluorophenyl derivative (III): in molecule 1 (Fig. 1*c*) the fluoro substituent is on the same edge as the N—H bond, while in molecule 2, where the orientation of the fluorophenyl ring is disordered over two sets of sites (see §2.2), the major orientation (Fig. 1*d*) has the fluoro substituent on the opposite edge, so that these two conformers form a pair of conformational isomers: no such phenomenon is apparent in any of the other compounds having Z' = 2, particularly the 2-fluorophenyl isomer (II). In each of the two 2-alkoxyphenyl compounds (XI) and (XIV), both independent molecules have the 2-alkoxy substituent on the same edge as the N—H bond, while each of the 3-alkoxyphenyl compounds (XII) and (XV) have the substituent on the edge opposite the N—H bond: the same substituent location was found in the dihydrate (XI*a*) (Qiu, Xu *et al.*, 2006), although the unique organic component was found to be almost perfectly planar, by contrast with the molecules in (XI).

Finally we note that in (I) and (X) the two independent molecules selected to form the asymmetric units are almost, although not exactly, enantiomeric; however, the conformations of the independent molecules in the selected asymmetric units of (II), (XI) and (XIV) differ rather too much for these to be regarded as even approximately enantiomeric.

3.4. Supramolecular structures

We shall analyse the supramolecular aggregation of the unsubstituted parent compound (I) in some detail, followed by a comparison of the geometric isomers of each of the substituted types. The direction-specific interactions which are

Table 3
Hydrogen-bond parameters (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
(I)				
N17—H17···N31	0.88	2.22	3.080 (2)	166
N37—H37···N11^{i}	0.88	2.22	3.076 (2)	163
C12—H12···Cg1^{ii}†	0.95	2.77	3.517 (2)	137
C16—H16···Cg2^{iii}‡	0.95	2.89	3.610 (2)	134
C26—H26···Cg3^{iii}§	0.95	2.99	3.581 (2)	121
C43—H43···Cg4^{iv}¶	0.95	2.89	3.610 (2)	134
(II)				
N17—H17···N31	0.90	2.21	3.0895 (19)	165
N37—H37···N11^{v}	0.90	2.19	3.0700 (19)	165
C13—H13···N31	0.95	2.53	3.463 (2)	167
(III)				
N17—H17···O3	0.88	2.09	2.937 (2)	162
N37—H37···N27^{vi}	0.88	2.53	3.381 (2)	162
C24—H24···N31^{vii}	0.95	2.59	3.517 (3)	166
C44—H44···N11^{viii}	0.95	2.48	3.414 (3)	167
(IV)				
N17—H17···O2	0.90	1.93	2.8059 (18)	165
O2—H2A···N11^{vii}	0.84	2.02	2.833 (2)	163
O2—H2B···O1^{ix}	0.84	2.26	2.9354 (19)	137
O2—H2B···N27^{ix}	0.84	2.52	3.2427 (18)	145
(V)				
N17—H17···N11^{x}	0.88	2.05	2.9231 (18)	175
C23—H23···O1^{xi}	0.95	2.51	3.2218 (19)	132
C16—H16···Cg3^{vii}§	0.95	2.85	3.723 (2)	154
(VI)				
N17—H17···N11^{xii}	0.88	2.25	3.0776 (18)	156
C12—H12···O1^{xiii}	0.95	2.43	3.316 (2)	154
(VIII)				
N17—H17···N11^{x}	0.96	2.00	2.955 (3)	172
C23—H23···O1^{xi}	0.95	2.52	3.213 (4)	130
C16—H16···Cg3^{vii}§	0.95	2.87	3.743 (3)	154
(IX)				
N17—H17···N11^{xii}	0.88	2.27	3.117 (2)	163
C12—H12···O1^{xiii}	0.95	2.48	3.371 (2)	156
(X)				
N17—H17···O2	0.88	2.03	2.864 (7)	159
N37—H37···O4	0.88	1.96	2.834 (7)	171
O2—H2A···O3	1.00	2.05	2.848 (7)	135
O2—H2A···N47	1.00	2.40	3.287 (7)	148
O2—H2B···N11^{xiv}	1.00	2.00	2.944 (7)	156
O4—H4A···N31^{ii}	1.00	1.85	2.789 (7)	155
O4—H4B···O1^{xv}	1.00	2.10	2.867 (7)	132
C13—H13···O2	0.95	2.48	3.327 (8)	149
C27—H27···O2	0.95	2.45	3.249 (8)	142
C33—H33···O4	0.95	2.45	3.191 (8)	135
(XI)				
N17—H17···O3	0.88	2.05	2.8239 (16)	147
N17—H17···N47	0.88	2.51	3.2440 (18)	141
N37—H37···O1^{xvi}	0.88	2.06	2.7757 (16)	138
C33—H33···O1^{xvi}	0.95	2.34	3.2550 (19)	163
C47—H47···O1^{xvi}	0.95	2.43	3.1243 (19)	130
(XII)				
N17—H17···N11^{xii}	0.88	2.24	3.044 (2)	152
C12—H12···O1^{xiii}	0.95	2.40	3.227 (3)	145
C24—H24···N27^{xvii}	0.95	2.57	3.480 (3)	161
C27—H27···N11^{xii}	0.95	2.58	3.353 (3)	139
C16—H16···Cg2^{xviii}‡	0.95	2.92	3.689 (2)	139
(XIII)				
N17—H17···O2	0.88	2.03	2.907 (2)	173

Table 3 (continued)

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2A···N11^{xix}	0.90	1.90	2.794 (2)	176
O2—H2B···O1^{viii}	0.90	1.95	2.846 (2)	176
(XIV)				
N17—H17···O3	0.88	1.99	2.836 (2)	160
N37—H37···O1^{xvi}	0.88	2.01	2.879 (2)	168
C27—H27···O3	0.95	2.60	3.352 (2)	136
C33—H33···O1^{xvi}	0.95	2.38	3.238 (2)	150
C47—H47···O1^{xvi}	0.95	2.47	3.287 (2)	145
(XV)				
N17—H17···O1^{xix}	0.88	2.08	2.898 (3)	154
C12—H12···N11^{xx}	0.95	2.52	3.424 (3)	160

Symmetry codes: (i) $\frac{1}{2}-x,-\frac{1}{2}+y,z$; (ii) $-x,\frac{1}{2}+y,\frac{1}{2}-z$; (iii) $\frac{1}{2}+x,\frac{3}{2}-y,1-z$; (iv) $-x,-\frac{1}{2}+y,\frac{1}{2}-z$; (v) $x,1+y,z$; (vi) $-\frac{1}{2}+x,\frac{1}{2}-y,1-z$; (vii) $-x,\frac{1}{2}+y,\frac{3}{2}-z$; (viii) $1-x,\frac{1}{2}+y,\frac{1}{2}-z$; (ix) $-1+x,y,z$; (x) $1+x,y,z$; (xi) $x,\frac{1}{2}-y,-\frac{1}{2}+z$; (xii) $\frac{1}{2}-x,\frac{1}{2}+y,\frac{1}{2}-z$; (xiii) $-\frac{1}{2}+x,\frac{1}{2}-y,-\frac{1}{2}+z$; (xiv) $1-x,\frac{1}{2}+y,\frac{3}{2}-z$; (xv) $-1+x,\frac{1}{2}-y,-\frac{1}{2}+z$; (xvi) $1-x,-\frac{1}{2}+y,\frac{1}{2}-z$; (xvii) $\frac{1}{2}-x,\frac{1}{2}+y,\frac{3}{2}-z$; (xviii) $\frac{1}{2}+y,\frac{1}{2}-y,-\frac{1}{2}+z$; (xix) $x,\frac{3}{2}-y,\frac{1}{2}+z$; (xx) $1-x,-\frac{1}{2}+y,\frac{3}{2}-z$. † Cg1 is the centroid of ring (C41–C46). ‡ Cg2 is the centroid of ring (C21–C26). § Cg3 is the centroid of ring (N11, C12–C16). ¶ Cg4 is the centroid of ring (N31, C32–C36).

apparent within this series include hydrogen bonds of N—H···N, N—H···O, C—H···N, C—H···O and C—H···π(arene) types, together with O—H···O and O—H···N types in the hydrates (IV), (X), (XIII) and (XX), along with $\pi\cdots\pi$ stacking interactions. Cogent criticism of the progres-

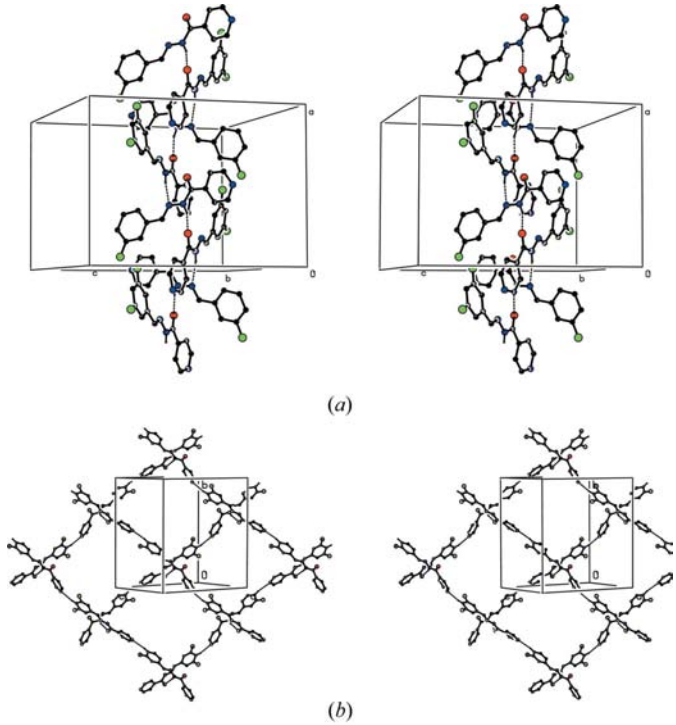


Figure 4
Stereoviews of parts of the crystal structure of the 3-fluorophenyl compound (III) showing (*a*) the formation of a $C_2^2(7)$ chain along [100] built from N—H···O and N—H···N hydrogen bonds, and (*b*) the formation of an $R_8^8(64)$ sheet parallel to (101) built from N—H···O and C—H···N hydrogen bonds. For the sake of clarity, the minor orientation of the disordered type 2 molecule and the H atoms not involved in the motifs shown have been omitted.

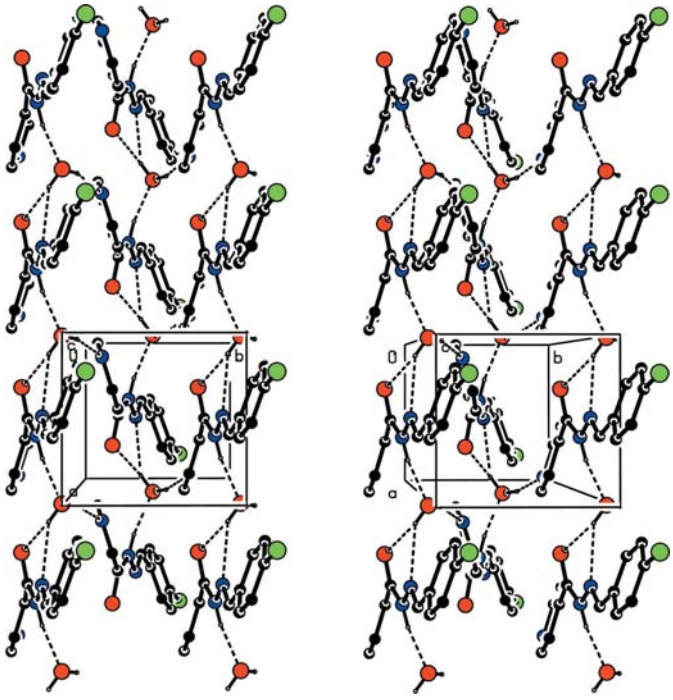


Figure 5
A stereoview of part of the crystal structure of the hydrated 4-fluorophenyl compound (IV) showing the formation of a sheet parallel to (001). For the sake of clarity the H atoms not involved in the motifs shown have been omitted.

sive relaxation of the definition of, and criteria for, significant hydrogen bonds (Cotton *et al.*, 1997) makes it desirable to specify the acceptance criteria for the hydrogen bonds considered in this study (Table 3). Of the interactions labelled as 'potential hydrogen bonds' by *PLATON* (Spek, 2003), we have discounted the following intermolecular interactions:

(i) C—H···O contacts in which the H···O distance exceeds 2.55 Å, and/or the C—H···O angle is less than 130°;

(ii) all C—H···O and C—H···π(arene) contacts in which the C—H bond is part of the methyl group, as it has been shown by solid-state NMR spectroscopy (Riddell & Rogerson, 1996, 1997) that methyl groups CH_3-*E* generally undergo very rapid rotation about the C—*E* bond even at low temperatures in the solid state, so that the apparent H-atom sites in effect represent not static positions, but merely the energy minima of the rotational potential-energy function; and

(iii) the C—H···F—C contacts in (III) and (IV), where the F is known (Brammer *et al.*, 2001) to be an extremely weak acceptor, and where the likelihood is that these contacts are associated with interaction energies which are, at best, negligibly attractive and which are probably repulsive at most geometries (Howard *et al.*, 1996).

3.4.1. The unsubstituted parent compound (I). The molecules of (I) are linked into chains by two independent N—H···N hydrogen bonds (Table 3), and these chains are further linked into a three-dimensional framework by a combination of C—H···π(arene) and C—H···π(pyridyl) hydrogen bonds

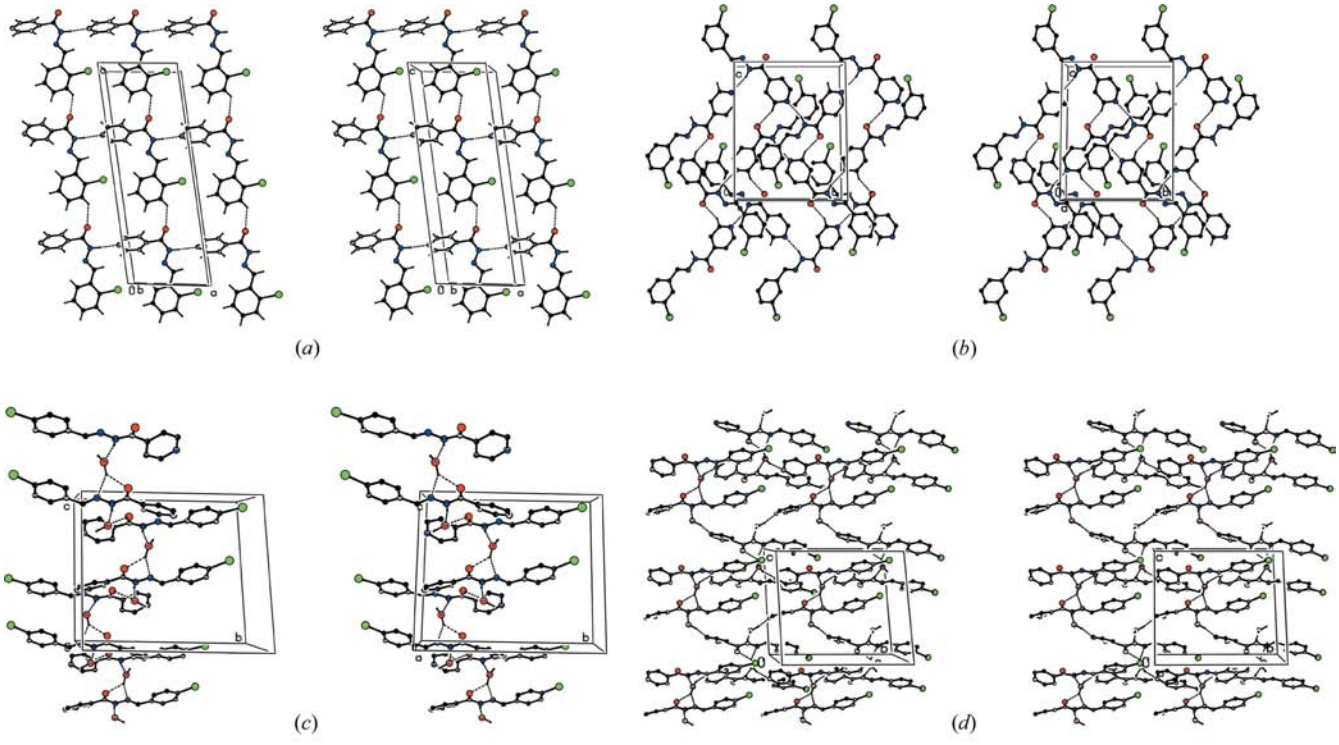


Figure 6
Stereoviews of parts of the crystal structures of (*a*) the 2-bromophenyl compound (VIII) showing the formation of hydrogen-bonded *C*(7) and *C*(9) chains along [100] and [001]; (*b*) the 3-bromophenyl compound (IX) showing the combination of hydrogen-bonded *C*(7) and *C*(6) chains along [100] and [101] to form a sheet of alternating $R_4^4(16)$ and $R_4^4(30)$ rings; and the hydrated 4-bromophenyl compound (X) showing (*c*) a chain parallel to [201] and (*d*) a sheet parallel to (10$\bar{1}$). For the sake of clarity the H atoms not involved in the motifs shown have been omitted.

(Table 3). Within the selected asymmetric unit, the N17 atom acts as a hydrogen-bond donor to the pyridyl N31 atom, while the N37 atom similarly acts as a donor to the pyridyl N11 atom at $(\frac{1}{2}-x, -\frac{1}{2}+y, z)$, so forming a $C_2^2(14)$ (Bernstein *et al.*, 1995) chain running parallel to the [010] direction and generated by the *b* glide plane at $x = 0.25$ (Fig. 2*a*). Four chains of this type pass through each unit cell and their linking into a three-dimensional framework can conveniently be analysed in terms of two pairs of C—H···π hydrogen bonds. The pyridyl C12 atom at (x, y, z) acts as a donor to the arene ring (C41–C46) at $(-x, \frac{1}{2}+y, \frac{1}{2}-z)$, while the aryl C43 atom at (x, y, z) acts as a donor to the pyridyl ring (N31,C32–C36) at $(-x, -\frac{1}{2}+y, \frac{1}{2}-z)$: these two hydrogen bonds together form a ladder motif running parallel to the [010] direction and generated by the 2_1 screw axis along $(0, y, 0.25)$. Similarly, the C16 and C26 atoms at (x, y, z) act as donors, respectively, to the rings (C21–C26) and (N11,C12–C16), both at $(\frac{1}{2}, \frac{3}{2}-y, 1-z)$, so forming a second ladder, this time parallel to the [100] direction and generated by the 2_1 screw axis along $(x, 0.75, 0.5)$. The combination of these three chain motifs suffices to generate a three-dimensional framework, whose formation can be envisaged as follows: the combination of the two [010] motifs generates a sheet parallel to (001) (Fig. 2*a*), while successive molecules in the [100] ladder (Fig. 2*b*) lie in adjacent (001) sheets, thus linking these sheets.

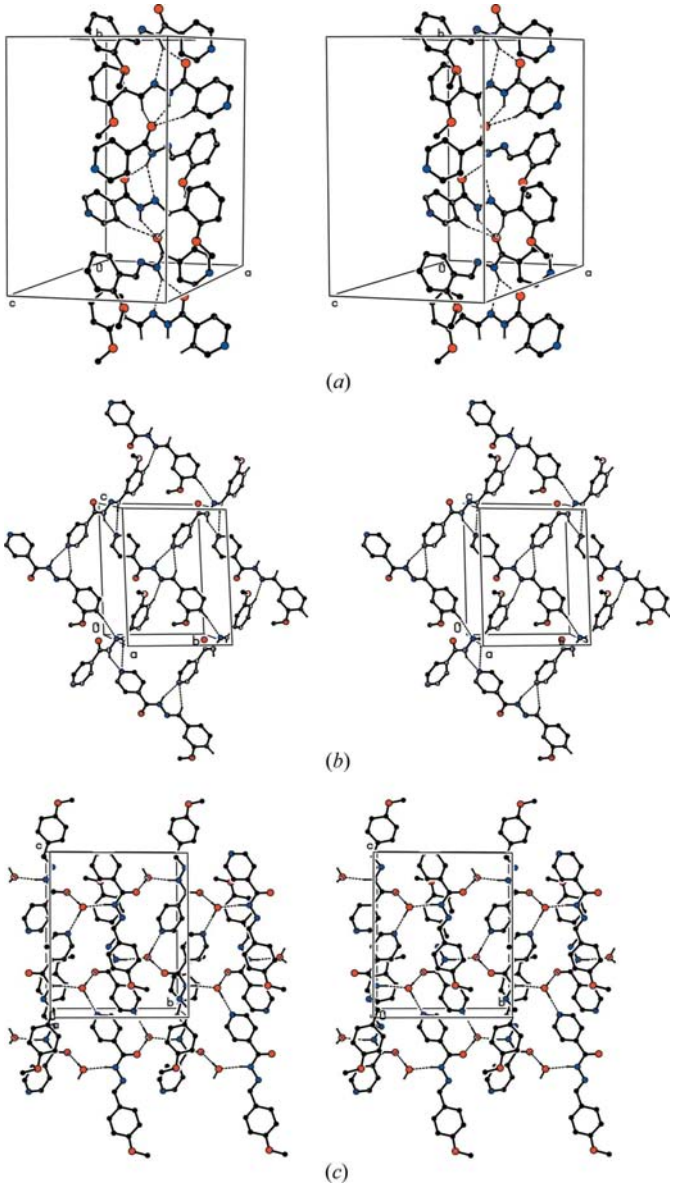


Figure 7
Stereoviews of parts of the crystal structures of (*a*) the 2-methoxyphenyl compound (XI) showing the formation of a chain of rings along [010]; (*b*) the 3-methoxyphenyl compound (XII) showing the formation of a sheet of $R_2^1(5)$ and $R_4^4(28)$ rings parallel to (100); and (*c*) the hydrated 4-methoxyphenyl compound (XIII) showing the formation of a sheet of $R_4^4(18)$ and $R_8^8(30)$ rings parallel to (100). For the sake of clarity the H atoms not involved in the motifs shown have been omitted.

3.4.2. The fluorophenyl derivatives (II)–(IV). The 2-, 3- and 4-fluorophenyl derivatives (II), (III) and (IV), the last of which is a stoichiometric monohydrate (see §3.1) all crystallize in different space groups (Table 1), with Z' values of 2, 2 and 1, respectively. The hydrogen-bonded supramolecular structures are respectively one-dimensional, three-dimensional and two-dimensional.

In the 2-fluorophenyl compound (II), a combination of one C—H···N and two N—H···N hydrogen bonds links the two independent molecules into a $C_2^2(11)C_2^2(14)[R_2^1(7)]$ chain of rings running parallel to the [010] direction (Fig. 3*a*). Pairs of such chains related to one another by inversion, and hence running antiparallel, are linked by a single $\pi\cdots\pi$ stacking interaction. The pyridyl and aryl rings of the type 1 molecules at (x, y, z) and $(1-x, 1-y, 1-z)$, respectively, are almost parallel with a dihedral angle between them of only 0.5 (2)°: the ring centroid separation is 3.639 (2) Å and the interplanar spacing is *ca* 3.390 Å, corresponding to an almost ideal ring offset of *ca* 1.33 Å.

The supramolecular aggregation of the 3-fluorophenyl isomer (III) is much more complex than that of (II), and it depends on a combination of strong N—H···O and N—H···N hydrogen bonds and two weaker C—H···N hydrogen bonds (Table 3). The formation of the three-dimensional framework structure is readily analysed in terms of two simple substructures, one of them one-dimensional and built from the strong

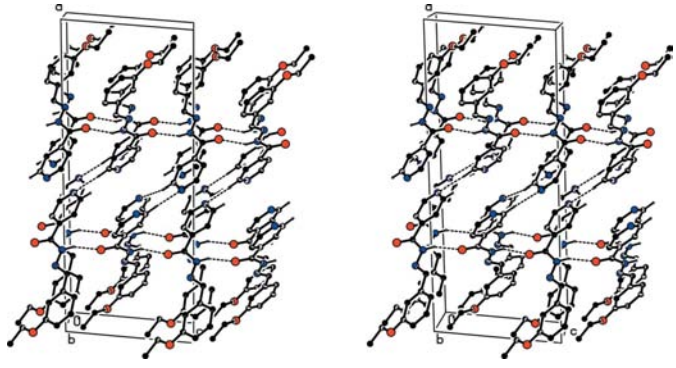


Figure 8
A stereoview of part of the crystal structure of the 3-ethoxyphenyl compound (XV) showing the formation of a sheet of $R_4^4(26)$ rings parallel to (100). For the sake of clarity the H atoms not involved in the motif shown have been omitted.

hydrogen bonds, and the other two-dimensional and utilizing the C—H···N hydrogen bonds. The N—H···O and N—H···N hydrogen bonds together produce a $C_2^2(7)$ chain running parallel to the [100] direction and generated by the 2_1 screw axis along (x, 0.25, 0.5) (Fig. 4*a*). The two C—H···N hydrogen bonds, together with the N—H···O hydrogen bond within the asymmetric unit, give rise to a sheet of $R_8^8(64)$ rings lying parallel to (101) (Fig. 4*b*). The combination of [010] chains and (101) sheets suffices to generate a single three-dimensional framework. This framework is reinforced by a single $\pi\cdots\pi$ stacking interaction between the pyridyl rings (N11, C12–C16) of the type 1 molecules at (x, y, z) and ($1-x$, $-y$, $1-z$): the interplanar spacing is 3.412 (2) Å and the ring–centroid separation is 3.678 (2) Å, corresponding to a ring offset of 1.373 (2) Å.

The 4-fluorophenyl compound (IV) crystallizes as a stoichiometric monohydrate but, despite this, the supramolecular aggregation is only two-dimensional; as such, it contrasts with the aggregation in the two isomeric compounds (II) and (III). The two molecular components are linked within the selected asymmetric unit by an N—H···O hydrogen bond, and these bimolecular units are themselves linked by a two-centre O—H···N hydrogen bond and by a rather asymmetric three-centre O—H···(N,O) hydrogen bond. However, by contrast with isomers (II) and (III), C—H···N hydrogen bonds are absent from the structure of (IV), as are C—H···O hydrogen bonds. The two-centre O—H···N hydrogen bond, in combination with the N—H···O hydrogen bond within the asymmetric unit, gives rise to a $C_2^2(9)$ chain running parallel to the [010] direction, and generated by the 2_1 screw axis along (0, y, 0.75). The three-centre hydrogen bond generates by translation a $C_2^2(5)C_2^2(6)[R_1^2(5)]$ chain of rings running parallel to [100], and the combination of the chains along [100] and [010] generates a sheet parallel to (001) (Fig. 5). Two sheets, related to one another by inversion, pass through each unit cell, but there are no direction-specific interactions between adjacent sheets, nor is there any interweaving of the sheets.

3.4.3. The chlorophenyl and bromophenyl derivatives (V)–(X). As noted above (§3.1) the 2-chlorophenyl and 3-chlorophenyl derivatives (V) and (VI) are isostructural with the bromo-substituted analogues (VIII) and (IX) (Tables 1 and 3), and for each isomer the molecular volumes of the chloro and bromo analogues are surprisingly similar. We have not been able to crystallize the 4-chloro compound (VII) and, while it is a reasonable inference that this might be isostructural with the 4-bromophenyl compound (X), this can only be conjecture at this stage. The supramolecular aggregation of the 2-substituted forms (V) and (VIII) is three-dimensional, as is that of the hydrate of the 4-bromo compound (X), while the supramolecular aggregation of the 3-substituted isomers (V) and (IX) is only two-dimensional. Owing to the isostructural relationships, we only discuss here the supramolecular aggregation of the three isomeric bromo compounds.

In the 2-bromophenyl compound (VIII), N—H···N, C—H··· and C—H···π(pyridyl) hydrogen bonds (Table 3) respectively generate chains parallel to the [100], [001] and [010] directions, and the combination of these chains generates a single three-dimensional framework. The chains along [100] and [001] are, respectively, of $C(7)$ and $C(9)$ types (Fig. 6*a*), and together they generate a sheet of $R_4^4(30)$ rings lying parallel to (010).

The molecules of the 3-bromophenyl isomer (IX) are again linked by N—H···N and C—H···O hydrogen bonds, although C—H···π interactions are absent. The two hydrogen bonds again link the molecules into chains of $C(7)$ type along [010] and of $C(6)$ type along [101], and these combine to form a sheet, this time parallel to (10$\bar{1}$) and now built from two types of ring, both centrosymmetric, with homodromic (Saenger, 1979; Jeffery & Saenger, 1991; Kálmán *et al.*, 2004) $R_4^4(14)$ rings and heterodromic $R_4^4(30)$ rings alternating in a chessboard fashion (Fig. 6*b*). There is a weak $\pi\cdots\pi$ stacking interaction within this sheet, but there are no direction-specific interactions between adjacent sheets; nor is there any interweaving of the sheets.

There are four independent molecular components in the monohydrate of the 4-bromophenyl compound (X) and within the selected asymmetric unit (Fig. 1*g*), these components are linked by two two-centre N—H···O hydrogen bonds and one three-centre O—H···(O,N) hydrogen bond, weakly reinforced by three C—H···O hydrogen bonds (Table 3). There are thus just three hydrogen bonds remaining, one of O—H···O type and two of O—H···N type, which we refer to as the 'exterior' hydrogen bonds, and these link the four-component aggregates together and thereby form a three-dimensional framework. The formation of the framework is most simply analysed in terms of two substructures, one of them one-dimensional and involving the exterior O4—H4*B*···O1 hydrogen bond, while the other is two-dimensional and involves the two exterior O2—H2*B*···N11 and O4—H4*A*···N31 hydrogen bonds (Table 3).

In the first substructure, the water O4 atom at (x, y, z) acts as a hydrogen-bond donor to the amide O1 atom at ($-1+x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$), so generating a $C_4^4(11)C_4^4(12)[R_1^2(5)]$ chain of rings parallel to the [201] direction (Fig. 6*c*). In the second substructure, the water O2 and O4 atoms at (x, y, z) act as donors, respectively, to the pyridyl atom N11 at ($1-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$) and N31 at ($-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$). Individually these interactions generate two independent $C_2^2(9)$ chains along (0.5, y, 0.75) and (0, y, 0.25), respectively, and together they generate a sheet parallel to (10$\bar{1}$) (Fig. 6*d*). The combination of [201] chains and (10$\bar{1}$) sheets suffices to generate a three-dimensional structure of considerable complexity.

3.4.4. The alkoxyphenyl derivatives (XI)–(XV) and (XI*a*). The 2-methoxyphenyl derivative (XI) and the 2-ethoxyphenylderivative (XIV) both crystallize in the space group $P2_1/c$ with Z' = 2. The unit-cell dimensions are somewhat similar apart from a significantly larger b value for (XIV). The corresponding atomic coordinates for the two compounds are approximately related by the transformation (x, y, $\frac{1}{2}-z$), and this approximate mirror-image relationship is manifested in the corresponding torsional angles (Table 2). The pattern and the dimensions of the significant hydrogen bonds [the first four entries in Table 3 for each of (XI) and (XIV)] match very closely, although in each compound there is an additional, and

possibly adventitious, weak interaction (the final entries in Table 3 for these compounds) which differ between the two. Owing to the close structural similarity between compounds (XI) and (XIV), we concentrate the discussion here on (XI).

Within the selected asymmetric unit of (XI), the molecular components are linked by an N—H···O hydrogen bond, possibly augmented albeit weakly by a long N—H···N interaction, so that these two together could be regarded as a very asymmetric three-centre N—H···(O,N) system. These two-component units are then linked into a complex chain of rings along [010] (Fig. 7*a*) by a combination of one N—H···O and two C—H···O hydrogen bonds. An exactly similar three-point linkage occurs in (XIV), and the principal difference between the aggregation of (XI) and (XIV) is that in (XIV) the N—H···N interaction within the asymmetric unit is replaced by a long C—H···O contact. In addition, the chains in (XI) are weakly linked by a $\pi\cdots\pi$ stacking interaction involving the pyridyl rings of the type 1 molecules. These rings at (x, y, z) and $(1-x, 1-y, 1-z)$ are strictly parallel with an interplanar spacing of 3.417 (2) Å; the ring-centroid separation is 3.725 (2) Å, corresponding to a ring-centroid offset of 1.483 (2) Å: however, this interaction is absent from the structure of (XIV).

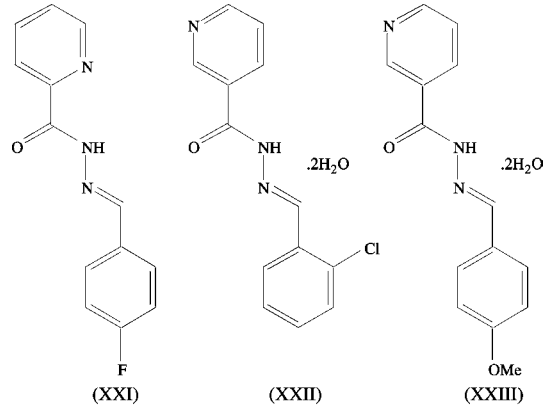
By contrast with the 2-alkoxy compounds (XI) and (XIV) the 3-substituted isomers (XII) and (XV) crystallize with very different unit-cell dimensions (Table 1) and their structures exhibit very different patterns of hydrogen bonds (Table 3); the supramolecular aggregation is three-dimensional in (XII), but only two-dimensional in (XV). In the 3-methoxy compound (XII), a combination of one N—H···N and two C—H···N hydrogen bonds links the molecules into sheets of $R_2^1(5)$ and $R_4^4(28)$ rings lying parallel to (100) (Fig. 7*b*), while the C—H···O hydrogen bond gives rise to a simple $C(6)$ chain running parallel to the [101] direction. The combination of [101] chains and (100) sheets generates a three-dimensional framework structure. The supramolecular aggregation in the 3-ethoxyphenyl compound (XV), by contrast, is very simple. The atoms H17 and H12 in the molecule at (x, y, z) act as hydrogen-bond donors, respectively, to the O1 and N11 atoms in the molecules at $(x, \frac{3}{2}-y, \frac{1}{2}+z)$ and $(1-x, -\frac{1}{2}+y, \frac{3}{2}-z)$, respectively. These interactions individually produce a $C(4)$ chain parallel to [001] and a $C(3)$ chain parallel to [010], and in combination they generate a sheet parallel to (100) containing two types of $R_4^4(26)$ ring, one of them homodromic and the other heterodromic (Fig. 8).

The supramolecular aggregation of the monohydrate of the 4-methoxyphenyl isomer (XIII) is very simple and depends on just three hydrogen bonds (Table 3). Within the selected asymmetric unit the molecular components are linked by an N—H···O hydrogen bond, and these units are then further linked by a combination of O—H···O and O—H···N hydrogen bonds. The water atom O2 at (x, y, z) acts as a hydrogen-bond donor *via* H2*A* and H2*B* to the atoms N11 at $(x, \frac{3}{2}-y, \frac{1}{2}+z)$ and O1 at $(1-x, \frac{1}{2}+y, \frac{1}{2}-z)$, thereby producing a $C_2^2(9)$ chain parallel to [001] generated by the *c* glide plane at $y = 0.75$ and a $C_2^2(6)$ chain parallel to [010] generated by the 2_1 screw axis along (0.5, *y*, 0.25). The combination of these two chains generates a sheet parallel to (100) built from alternating homodromic $R_8^8(39)$ rings and heterodromic $R_4^4(18)$ rings, where both types are centrosymmetric (Fig. 7*c*). There are no direction-specific interactions linking the (100) sheets.

As well as the solvent-free form (XI) reported here, a stoichiometric dihydrate (XI*a*) of the 2-methoxyphenyl derivative has been reported (Qiu, Xu *et al.*, 2006). These authors stated that the component molecules are linked through O—H···O and O—H···N hydrogen bonds. In fact, the structure contains an N—H···O hydrogen bond in addition to an O—H···N hydrogen bond and no fewer than three independent O—H···O hydrogen bonds. These interactions, in fact, link the molecules into complex sheets, but this is not obvious either from the authors' discussion or from their packing diagram, which shows only three of the five hydrogen bonds and appears, indeed, to omit one of the water molecules.

3.4.5. The nitrophenyl and cyanophenyl compounds (XVII)–(XX) and (XVIII*a*). In the isomeric nitrophenyl derivatives (XVII)–(XIX), the molecules are linked, respectively, into a three-dimensional framework by N—H···N and multiple C—H···O hydrogen bonds; into sheets by a combination of N—H···N, C—H···N and C—H···O hydrogen bonds; and into bilayers by a combination of N—H···N, C—H···N and two C—H···O hydrogen bonds (Wardell, de Souza, Wardell *et al.*, 2005). In the monohydrate (XVIII*a*), the components are linked into sheets by a combination of O—H···O, N—H···O, N—H···O and C—H···O hydrogen bonds (Wardell, Wardell *et al.*, 2007), while in the monohydrate (XX) a different combination of the same types of hydrogen bond links the molecular components into a three-dimensional framework structure (de Souza *et al.*, 2007).

3.4.6. Pyridyl isomers (XXI)–(XXIII). Here we comment briefly on three compounds (XXI)–(XXII) (see Scheme 3)



(XXI) (XXII) (XXIII)

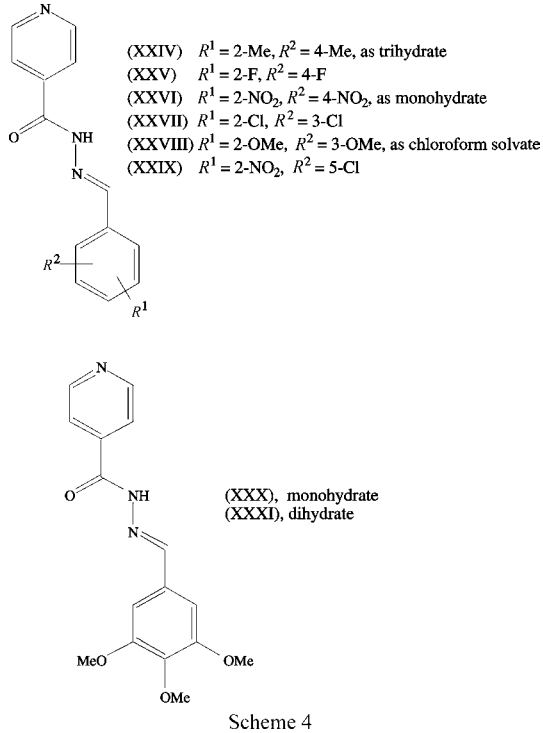
Scheme 3

where the hydrazone components are respectively isomers of the corresponding components in compounds (IV), (V) and (XIII), differing only in the position of the N atom of the pyridyl ring. None of the original reports on these compounds contains any detailed analysis of the supramolecular aggregation.

The report (Shao *et al.*, 2004) on 4-fluorobenzaldehyde picoloylhydrazone (XXI) makes no mention whatsoever

either of the hydrogen bonds or of the supramolecular aggregation. In the event, there is an intramolecular N—H···N hydrogen bond, which almost certainly plays a role in determining the molecular conformation, and precludes any participation by the N—H bond in intermolecular hydrogen bonds; the molecules are linked by a single C—H···O hydrogen bond into *C*(6) chains generated by translation along [100], and these are then linked into pairs by a single $\pi\cdots\pi$ stacking interaction. In the original report the packing diagram whose caption conveyed no useful information, was shown as a view along [100] thereby effectively obscuring the intermolecular hydrogen bond. The one-dimensional structure of (XXI) is thus markedly different from the three-dimensional structure of (IV). The structure of 2-chlorobenzaldehyde nicotinoylhydrazone dihydrate (XII) was described as column-like, but with the direction unspecified (Lu *et al.*, 1999). In fact, an extensive series of O—H···O, O—H···N and N—H···O hydrogen bonds link the molecular components into complex sheets parallel to (001). The report (Fun *et al.*, 1996) on 4-methoxybenzaldehyde nicotinoylhydrazone dihydrate (XXIII) noted that the structure is stabilized by extensive hydrogen bonding, but gave no further detail beyond a listing of the hydrogen bonds. In the event, the molecular components are linked into a three-dimensional framework structure, so that the hydrogen-bonded supramolecular aggregation in (XXI), (XXII) and (XXIII) is one-, two- and three-dimensional, respectively.

3.4.7. Di- and tri-substituted arylaldehyde analogues (XXIV)–(XXXI). Here we summarize briefly the supramolecular aggregation patterns in the disubstituted analogues (XXIV)–(XXIX) (see Scheme 4) and the two hydrates (XXX) and (XXXI) containing a trisubstituted aryl ring.



Scheme 4

The supramolecular structure of the trihydrate (XXIV), where there are methyl substituents in the 2- and 4- positions, is a three-dimensional framework built from N—H···O, O—H···O and O—H···N hydrogen bonds (Low *et al.*, 2006). By contrast, molecules of the 2,4-difluorophenyl analogue (XXV) are linked by a combination of N—H···O and C—H···O hydrogen bonds into chains of rings, which are themselves linked into sheets by a single $\pi\cdots\pi$ stacking interaction (Wardell, de Souza, Ferreira *et al.*, 2005). When the aryl substituents at positions 2 and 4 are nitro groups, the monohydrate (XXVI) forms a three-dimensional framework structure of some complexity involving N—H···O, O—H···O, O—H···N and three independent hydrogen bonds (Wardell, de Souza, Wardell *et al.*, 2005).

The molecules of the 2,3-dichlorophenyl derivative (XXVII) are linked by a combination of N—H···N, C—H···N and C—H···O hydrogen bonds into sheets of alternating $R_4^4(14)$ and $R_4^4(26)$ rings (Wardell, de Souza, Ferreira *et al.*, 2005), while those of the 2,3-dimethoxyphenyl compound (XXVIII) are linked by a combination of N—H···N and C—H···N hydrogen bonds into chains from which the chloroform solvate molecules are pendent. The molecules of the 5-chloro-2-nitrophenyl analogue (XXIX) are linked into a three-dimensional framework by one N—H···N hydrogen bond and three independent C—H···O hydrogen bonds (Wardell, de Souza, Wardell *et al.*, 2006).

The 3,4,5-trimethoxyphenyl compound forms two stoichiometric hydrates (XXX) and (XXXI) (Peralta *et al.*, 2007). In the monohydrate (XXX) the molecular components are linked into sheets by a combination of O—H···O, O—H···N and N—H···N hydrogen bonds, while in the dihydrate (XXXI), a combination of N—H···O, O—H···O and O—H···N hydrogen bonds links the components into a three-dimensional framework structure.

3.5. Conformations and intermolecular interactions

It is tempting to consider the differing molecular conformations observed here (Table 2) in the context of the direction-specific intermolecular forces, in particular the hydrogen bonds (Table 3). The isostructural pair of 2-halophenyl compounds (V) and (VIII) are the only examples here of *cis* amides (Fig. 1*e*), but the direction-specific intermolecular interactions manifested in their structures (N—H···N, C—H···O and C—H···π hydrogen bonds) differ little from those found in the structure of the 3-methoxyphenyl compound (XII) which, of course, adopts the *trans* amide conformation. On the other hand, the intermolecular interactions (N—H···N and C—H···O hydrogen bonds) found in the isostructural pair of 3-halophenyl compounds (VI) and (IX), where the halogen substituent is, unusually, on the same edge of the molecule as the carbonyl O atom, differ from those (N—H···O and C—H···N hydrogen bonds) in the 3-ethoxy compound (XV) which similarly has the ethoxy substituent on the same edge as the carbonyl O atom. Perhaps more unexpected is the observation that the two independent molecules of the 3-fluorophenyl compound (III) are conformational

isomers, with the fluoro substituent on opposite edges in the two molecules (Figs. 1*c* and *d*): while each conformational isomer acts as both a donor and an acceptor in C—H···N hydrogen bonds, the type 1 molecule also acts as a donor in an N—H···O hydrogen bond and as an acceptor in an N—H···N hydrogen bond, and conversely in the type 2 molecule. Even this small sample from the overall range of compounds discussed here indicates that the relationships between molecular conformation in the solid state and weak direction-specific intermolecular interactions are extremely subtle, such that no simple patterns can readily be discerned.

4. Concluding remarks

We comment briefly here on two aspects of the structures reported here and in earlier work, specifically involving solvation and the types and actions of the hydrogen bonds manifested in the structures.

Solvation: Amongst the structures reported in the present paper, crystallization as hydrates is restricted to (IV), (X) and (XIII), all of which crystallize as stoichiometric monohydrates: all of these compounds contain a substituent at the 4-position of the aryl ring. Similarly, the 4-cyano derivative (XX) also crystallizes as a stoichiometric monohydrate (de Souza *et al.*, 2007). While (IV), (X) and (XIII) were all prepared in aqueous solution, (X) was prepared in tetrahydrofuran and then crystallized from aqueous ethanol. Hence, the water component of these hydrates could be derived either from the solvent of preparation or from the solvent of crystallization. However, it may be noted that (I)–(III), (V), (VI), (VIII), (IX), (XI), (XII), (XIV) and (XV) were all prepared in exactly the same way as (IV), (X) and (XIII), and all were crystallized from solvents which normally contain modest quantities of water. Hence, we conclude that the formation or otherwise of hydrates is not simply a general consequence of the preparative regime, but a reflection of specific intermolecular interactions in some isomers but not others.

However, despite this apparent propensity amongst the 4-isomers to form hydrates there is, in fact, no necessary connection between the substituent location and the degree of solvation. Thus, the 2-methoxy compound (XI), crystallized here from methanol in solvent-free form, has also been reported as the dihydrate (XI*a*), crystallized from 95% aqueous ethanol (Qiu, Xu *et al.*, 2006), while the 3-nitro compound can be crystallized in the solvent-free form (XVIII) from methanol (Wardell, de Souza, Wardell *et al.*, 2005) and as the monohydrate (XVIII*a*) from ethanol (Wardell, Wardell *et al.*, 2007). Similarly, although the 2-pyridyl-4-fluoro compound (XXI) crystallizes from methanol in solvent-free form (Shao *et al.*, 2004), the 3-pyridyl-2-chloro derivative (XXII) (Lu *et al.*, 1999) and the 3-pyridyl-4-methoxy derivative (XXIII) (Fun *et al.*, 1996) both crystallize from ethanol as stoichiometric dihydrates. In these examples there appears to be a clear effect of the crystallization solvent on the solvation status of the product.

The patterns of solvation become more complex when multiple substituents are present in the aryl ring. Thus, the 2,4-dinitrophenyl compound (XXVI) crystallizes from methanol as a monohydrate (Wardell, de Souza, Wardell *et al.*, 2005), while the 2,4-dimethylphenyl compound (XXIV) crystallizes from ethanol as a trihydrate (Low *et al.*, 2006): these derivatives both carry a substituent in the 4-position of the aryl ring, but the corresponding 2,4-difluorophenyl compound (XXV) with the same pattern of substitution as compounds (XXIV) and (XXVI) crystallizes from ethanol in solvent-free form, in contrast to the 4-fluorophenyl compound (IV), which forms a monohydrate when crystallized from ethanol. The 3,4,5-trimethoxyphenyl compound forms two stoichiometric hydrates, a dihydrate (XXXI) obtained from ethanol solutions and a monohydrate (XXX) obtained by crystallizing the dihydrate from chloroform/propan-2-ol solutions (Peralta *et al.*, 2007). Crystals of the 2,3-dimethoxyphenyl analogue (XXVIII) grown from either methanol or ethanol were found to be unsuitable for single-crystal X-ray diffraction (Peralta *et al.*, 2007), but crystallization from chloroform gave good crystals of the stoichiometric chloroform monosolvate.

While, in general, the formation of hydrates is more frequently observed in products crystallized from ethanol than in those crystallized from methanol, the example of the 2,4-difluorophenyl compound (XXV) contradicts this general trend. Moreover, it should be noted firstly that the hydrates observed throughout this series are all stoichiometric mono-, di- or trihydrates, and secondly that in every such hydrate the water component is tightly integrated into the supramolecular network as both a hydrogen-bond donor and a hydrogen-bond acceptor. In no case can the formation of a hydrate be regarded as a mere incidental or adventitious occurrence: the water components form an integral part of the supramolecular structures. Even in the chloroform solvate (XXVIII) the chloroform molecule is linked to the hydrazone component by hydrogen bonds.

A number of common patterns can be discerned in the hydrogen-bonded structures discussed in this work: we consider firstly the strong hydrogen bonds and then the weak ones.

(i) Strong hydrogen bonds. Amongst the unsolvated structures, the N—H bond forms a hydrogen bond with a pyridyl N atom as the acceptor in each of compounds (I), (II), (V), (VI), (VIII), (IX), (XII), (XVII), (XVIII), (XIX), (XXVII) and (XXIX), while the N—H bond forms a hydrogen bond with a carbonyl O atom as the acceptor in each of compounds (III), (XI), (XIV), (XV) and (XXV), suggesting a clear preference for a pyridyl N over carbonyl O as the acceptor. Amongst the hydrated structures, the formation of N—H···O hydrogen bonds with a water O atom as the acceptor is the predominant mode of association, occurring in each of compounds (IV), (X), (XI*a*), (XIII), (XVIII*a*), (XX), (XXIV) and (XXVI). The water O atoms in turn generally act as hydrogen-bond donors to both pyridyl N atoms and carbonyl O atoms, with no clear preference discernible.

In all of the unsolvated structures discussed here, the strong hydrogen bonds of N—H···N and/or N—H···O types generate chain structures, with the single exception of (XXI) whose structure contains no strong intermolecular hydrogen

bonds. In the hydrates, whose structures necessarily contain more hydrogen-bond donors and acceptors than are present in the anhydrous compounds, the strong hydrogen bonds combine to generate two-dimensional aggregation in (IV), (XI*a*), (XIII), (XVIII*a*), (XXII), (XXV) and (XXX), and three-dimensional aggregation in (X), (XX), (XXIII), (XXIV) and (XXXI). In the few examples where different degrees of hydration of a common organic component have been observed, there appears to be an increase in the dimensionality of the aggregation generated by the strong hydrogen bonds as the degree of hydration increases. Thus, while the strong hydrogen bonds in the anhydrous compounds (XI) and (XVIII) generate one-dimensional structures, in the hydrates (XI*a*) and (XVIII*a*) these interactions generate two-dimensional structures: similarly, the strong hydrogen bonds generate a three-dimensional structure in the monohydrate (XXX), but a three-dimensional structure in the corresponding dihydrate (XXXI). It must, however, be emphasized that the number of examples here is very small.

(ii) Weak hydrogen bonds. We compare here the occurrence of weak hydrogen bonds in the unhydrated compounds only; in the hydrates, the presence of the water molecules effectively saturates the significant hydrogen-bond acceptor capacity. Weak hydrogen bonds of C—H$\cdots$O type only are present in each of compounds (V), (VI), (IX), (XI), (XIV), (XVII), (XXV) and (XXIX); weak hydrogen bonds of C—H$\cdots$N type only are present in each of compounds (II), (III) and (XV); while a combination of C—H$\cdots$O and C—H$\cdots$N hydrogen bonds is present in each of compounds (XVIII), (XIX) and (XXVII). Hydrogen bonds of C—H$\cdots\pi$ type are found only in (I), (V) and (VIII); (VIII) contains both C—H$\cdots$O and C—H$\cdots\pi$ hydrogen bonds; and (XII) contains hydrogen bonds of all three types.

Where one-dimensional structures are generated by the strong hydrogen bonds in anhydrous compounds, the resulting chains are generally further linked by the weak hydrogen bonds and $\pi\cdots\pi$ stacking interactions to form two-dimensional structures in (VI), (IX), (XIV), (XV), (XVIII), (XIX), (XXV) and (XXVII), and three-dimensional structures in (I), (III), (V), (VIII), (XII), (XVII) and (XXIX). The contrasts within the pairs of isomers (V) and (VI), (VII) and (IX), and (XI) and (XII) are noteworthy, as is the contrast between the three-dimensional structure of (XVII) and the two-dimensional structures of its isomers (XVII) and (XIX).

The diversity of the crystallization behaviour, and of the contribution of the strong and weak hydrogen bonds to the overall supramolecular aggregation, provides a significant challenge to any method attempting to predict molecular crystal structures from first principles. Convincing success in this area remains frustratingly elusive (Lommerse *et al.*, 2000; Motherwell, 2002; Day *et al.*, 2005). Any method which could encompass correctly the variations within the present series in terms of the variation in the aryl substituents, the isomerism in the aryl rings, and the isomerism in the pyridyl rings, as well as the solvation properties would represent an impressive advance.

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References

Bajue, S. A., Lewis, C., Clarke, K., Bramwell, F. B., Patrick, B. O. & Brock, C. P. (2003). *Acta Cryst.* C**59**, m207–m211.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Brammer, L., Bruton, E. A. & Sherwood, P. (2001). *Cryst. Growth Des.* **1**, 269–290.

Cotton, F. A., Daniels, L. M., Jordan, G. T. & Murillo, C. A. (1997). *Chem. Commun.* pp. 1673–1674.

Cuffini, S., Glidewell, C., Low, J. N., de Oliveira, A. G., de Souza, M. V. N., Vasconcelos, T. R. A., Wardell, S. M. S. V. & Wardell, J. L. (2006). *Acta Cryst.* B**62**, 651–665.

Day, G. M. *et al.* (2005). *Acta Cryst.* B**61**, 511–527.

Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.

Ferguson, G., Glidewell, C., Low, J. N., Skakle, J. M. S. & Wardell, J. L. (2005). *Acta Cryst.* C**61**, o445–o449.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Flack, H. D. (2003). *Helv. Chim. Acta*, **86**, 905–921.

Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.

Fun, H.-K., Sivakumar, K., Lu, Z.-L., Duan, C.-Y., Tian, Y.-P. & You, X.-Z. (1996). *Acta Cryst.* C**52**, 986–988.

Glidewell, C., Howie, R. A., Low, J. N., Skakle, J. M. S., Wardell, S. M. S. V. & Wardell, J. L. (2002). *Acta Cryst.* B**58**, 864–876.

Glidewell, C., Low, J. N., Skakle, J. M. S. & Wardell, J. L. (2005). *Acta Cryst.* C**61**, o312–o316.

Glidewell, C., Low, J. N., Skakle, J. M. S. & Wardell, J. L. (2006). *Acta Cryst.* B**62**, 666–675.

Glidewell, C., Low, J. N., Skakle, J. M. S., Wardell, S. M. S. V. & Wardell, J. L. (2005). *Acta Cryst.* B**61**, 227–237.

Hooft, R. W. W. (1999). *Collect.* Nonius BV, Delft, The Netherlands.

Howard, J. A. K., Hoy, V. J., O'Hagan, D. & Smith, G. T. (1996). *Tetrahedron*, **52**, 12613–12622.

Jeffrey, G. A. & Saenger, W. (1991). *Hydrogen Bonding in Biological Structures.* Berlin, Heidelberg: Springer Verlag.

Jing, Z.-L., Fan, Z., Yu, M., Chen, X. & Deng, Q.-L. (2005). *Acta Cryst.* E**61**, o3208–o3209.

Kálmán, A., Fábián, L., Argay, G., Bernáth, G. & Gyarmati, Z. C. (2004). *Acta Cryst.* B**60**, 755–762.

Kelly, C. J., Skakle, J. M. S., Wardell, J. L., Wardell, S. M. S. V., Low, J. N. & Glidewell, C. (2002). *Acta Cryst.* B**58**, 94–108.

Lommerse, J. P. M. *et al.* (2000). *Acta Cryst.* B**56**, 697–714.

Low, J. N., Wardell, S. M. S. V., de Souza, M. V. N., Wardell, J. L. & Glidewell, C. (2006). *Acta Cryst.* C**62**, o444–o446.

Lu, Z.-L., Kang, B.-S., Fun, H.-K., Razak, I. A. & Chinnakali, K. (1999). *Acta Cryst.* C**55**, 89–91.

McArdle, P. (2003). *OSCAIL for Windows*, Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.

Motherwell, W. D. S. *et al.* (2002). *Acta Cryst.* B**58**, 647–661.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, edited by C. W. Carter Jr & R. M. Sweet, Part A, pp. 307–326. New York: Academic Press.

Peralta, M. A., de Souza, M. V. N., Wardell, S. M. S. V., Wardell, J. L., Low, J. N. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o68–o72.

Qiu, X.-Y., Fang, X.-N., Yang, S.-L., Liu, W.-S. & Zhu, H.-L. (2006). *Acta Cryst.* E**62**, o2687–o2688.

Qiu, X.-Y., Xu, H.-J., Liu, W.-S. & Zhu, H.-L. (2006). *Acta Cryst.* E**62**, o2304–o2305.

Riddell, F. & Rogerson, M. (1996). *J. Chem. Soc. Perkin Trans. 2*, pp. 493–504.

Riddell, F. & Rogerson, M. (1997). *J. Chem. Soc. Perkin Trans. 2*, pp. 249–255.
Saenger, W. (1979). *Nature*, **279**, 343–344.
Shanmuga Sundara Raj, S., Fun, H.-K., Lu, Z.-L., Xiao, W., Tong, Y.-X. & Kang, B.-S. (1999). *Acta Cryst.* C**55**, 942–944.
Shao, S.-C., You, Z.-L., Fan, S.-H., Tang, L.-L., Lin, Y.-S. & Zhu, H.-L. (2004). *Acta Cryst.* E**60**, o2181–o2182.
Sheldrick, G. M. (1997*a*). *SHELXS*97. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXL*97. University of Göttingen, Germany.
Sheldrick, G. M. (2003). *SADABS*, Version 2.10. University of Göttingen, Germany.
Souza, M. V. N. de, Vasconcelos, T. R. A., Wardell, S. M. S. V., Wardell, J. L., Low, J. N. & Glidewell, C. (2005). *Acta Cryst.* C**61**, o204–o208.
Souza, M. V. N. de, Wardell, S. M. S. V., Wardell, J. L., Low, J. N. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o166–o168.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Wardell, J. L., Low, J. N., Skakle, J. M. S. & Glidewell, C. (2006). *Acta Cryst.* B**62**, 931–943.
Wardell, J. L., Wardell, S. M. S. V., Skakle, J. M. S., Low, J. N. & Glidewell, C. (2002). *Acta Cryst.* C**58**, o428–o430.
Wardell, S. M. S. V., de Souza, M. V. N., Ferreira, M. de L., Vasconcelos, T. R. A., Low, J. N. & Glidewell, C. (2005). *Acta Cryst.* C**61**, o617–o620.
Wardell, S. M. S. V., de Souza, M. V. N., Wardell, J. L., Low, J. N. & Glidewell, C. (2005). *Acta Cryst.* C**61**, o683–o689.
Wardell, S. M. S. V., de Souza, M. V. N., Wardell, J. L., Low, J. N. & Glidewell, C. (2006). *Acta Cryst.* E**62**, o3361–o3363.
Wardell, S. M. S. V., de Souza, M. V. N., Wardell, J. L., Low, J. N. & Glidewell, C. (2007). *Acta Cryst.* B**63**, 101–110.
Wardell, S. M. S. V., Wardell, J. L., Low, J. N., Glidewell, C. & de Souza, M. V. N. (2007). *Acta Cryst.* C**63**, o42–o44.
Wilson, A. J. C. (1976). *Acta Cryst.* A**32**, 994–996.
Yang, S., Zhang, S.-P., Wu, Y.-Y. & Shao, S.-C. (2006). *Acta Cryst.* E**62**, o28–o30.