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Patterns of hydrogen bonding in mono- and di-substituted *N*-arylpyrazinecarboxamides

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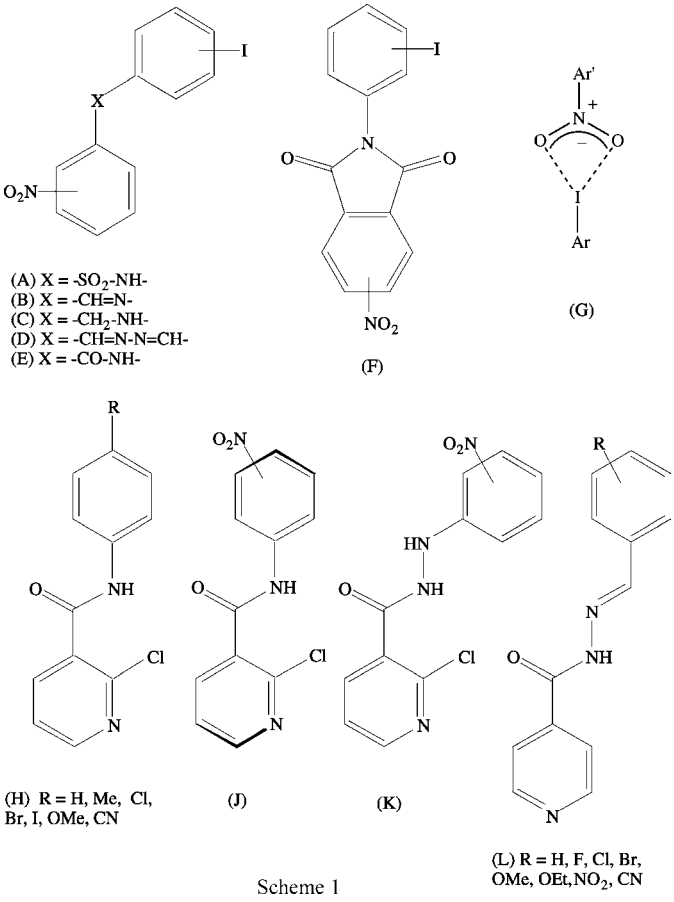
The molecular and supramolecular structures of 18 *N*-arylpyrazinecarboxamides, Ar NHCO($C_4H_3N_2$), have been determined, including the stoichiometric monohydrate of *N*-(3-methoxyphenyl)pyrazinecarboxamide, and two polymorphs of *N*-(4-fluorophenyl)pyrazinecarboxamide having Z' values of 1 and 4, respectively. The aryl groups were selected to include the geometric isomers for a compact range of substituents, namely methyl, trifluoromethyl, fluoro, chloro, methoxy and nitro groups, which exhibit markedly varied electronic properties and markedly varied behaviour as hydrogen-bond donors and acceptors. However, not all isomers in each group could be structurally investigated. A small number of derivatives containing disubstituted aryl groups have also been included in this study. The crystal structures of the solvent-free carboxamides reported here exhibit a wide range of direction-specific intermolecular forces, including N—H···N, N—H···O, C—H···N and C—H···O hydrogen bonds, and $\pi\cdots\pi$ stacking interactions, while the structure of *N*-(3-methoxyphenyl)pyrazinecarboxamide monohydrate also contains O—H···N and O—H···O hydrogen bonds. The resulting supramolecular structures can be zero-, one- or two-dimensional, although no three-dimensional supramolecular aggregation has been observed. In the finite, zero-dimensional structures, pairs of molecules are linked by hydrogen bonds to form cyclic centrosymmetric dimers. The one-dimensional structures include chains formed by the π-stacking of otherwise isolated molecules, simple chains generated by either C—H···O or C—H···N hydrogen bonds, and hydrogen-bonded chains of rings. The two-dimensional structures include examples of both π-stacked hydrogen-bonded chains and hydrogen-bonded sheets.

1. Introduction

We have, for a number of years, been interested in the interplay of various types of direction-specific intermolecular interactions. Many of our earlier studies in this area involved series of compounds in which two aryl units, one an iodophenyl ring and the other a nitrophenyl ring, are separated by a small spacer unit. Examples of this type include arenesulfonamides (*A*) (Kelly *et al.*, 2002), Schiff-base imines (*B*) (Glidewell *et al.*, 2002), benzylanilines (*C*) (Glidewell *et al.*, 2004), 2,3-diazabutadienes (*D*) (Glidewell, Low, Skakle & Wardell, 2005), benzamides (*E*) (Wardell *et al.*, 2006) and phthalimides (*F*) (Glidewell, Low, Skakle, Wardell & Wardell, 2005), permitting the formation of nine geometric isomers in each of these series apart from the phthalimides, where there are only six possible isomers. In general, we have found in each series of this type that every isomer exhibits a different pattern of supramolecular aggregation, often built from a

different selection of direction-specific intermolecular interactions such that the detailed structure of no one isomer could easily be predicted even given a detailed knowledge of the structure of every other isomer in the same series.



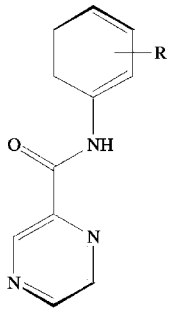
Scheme 1

The wide structural variability observed within each of these series presents major challenges for any computational methods, which attempt to predict molecular crystal structures from first principles (Lommerse *et al.*, 2000; Motherwell *et al.*, 2002; Day *et al.*, 2005). In the series in question, the unpredictable structural variability may be, at least in part, a consequence of the rather erratic behaviour, indeed the real unreliability, of the iodo···nitro synthon. A series of elegant structures containing symmetrical or nearly symmetrical three-centre interactions have been reported by others, the earlier examples serving as the archetypes for this interaction, which rapidly came to be regarded as a robust supramolecular synthon for crystal engineering (Allen *et al.*, 1994; Thalladi *et al.*, 1996; Masciocchi *et al.*, 1998; George *et al.*, 2004). However, these reports each refer to a single geometrical isomer and these structures all happen to involve molecular components with the substituents at the distal ends: this three-centre iodo–nitro interaction (*G*) appears to form reliably when the iodo and nitro substituents both occupy the 4 and 4′ positions as, for example, in the 1:1 adduct of 1,4-diiodobenzene and 1,4-dinitrobenzene (Allen *et al.*, 1994), in 4-iodonitrobenzene (Thalladi *et al.*, 1996), in 4-iodo-4′-nitrobiphenyl (Masciocchi *et al.*, 1998) and in *N*-4-iodophenyl-N′-4′-nitrophenylurea (George *et al.*, 2004). However, in examples where either substituent occupies the 2- or 3- positions, this interaction is generally absent (Wardell *et al.*, 2006). Thus, in substituted aryl systems the three-centre iodo···nitro synthon appears to behave predictably only for specific isomeric forms, but it is normally absent for the remaining isomeric forms.

Accordingly, we have in our more recent studies attempted to avoid the possible presence of this unpredictable iodo···nitro interaction. These studies have included those of two series of substituted 2-chloro-*N*-arylnicotinamides, one of them, series (*H*) (Cuffini *et al.*, 2006), was designed to investigate the effects of changing the identity of a single substituent as a fixed position, while in the second series (*J*) (de Souza *et al.*, 2005), a common substituent is located at three different positions. In series (*H*) the supramolecular aggregation is dominated by N—H···O=C hydrogen bonds forming $C(4)$ or $C_2^2(8)$ (Bernstein *et al.*, 1995) chains when R = Me, Cl, Br, I or OMe, although the methyl and chloro derivatives are not isostructural, but when R = H or CN the dominant intermolecular interactions are N—H···N(pyridyl) hydrogen bonds. However, the behaviour of the pyridyl N atom as a hydrogen-bond acceptor in this series appears to be somewhat capricious: it acts as an acceptor in an O—H···N hydrogen bond when R = F (this compound crystallizes as a monohydrate) and in a C—H···N hydrogen bond when R = Br, but it is wholly inactive as an acceptor when R = Me, Cl or I: no obvious pattern of behaviour is discernable here. In series (*J*), the 3-nitro isomer crystallizes as a monohydrate, but the molecules of the 2-nitro isomer are linked into a chain of edge-fused rings by two independent C—H···O hydrogen bonds, while those of the 4-nitro isomer (where Z' = 2) are linked into a simple $C_2^2(12)$ chain by two independent N—H···N hydrogen bonds: again no simple pattern is discernible. In the series of acylhydrazones (*K*) (Wardell *et al.*, 2007*a*), analogous to the amides in series (*J*), the 2-nitro isomer crystallizes in three polymorphic forms, in space groups *Cc*, $P2_1$ and *Pbcn*, respectively, in which the types of hydrogen bonds present in the three structures, and the supramolecular structures themselves are all completely different. While the hydrogen-bond types which are present in the structures of the 3-nitro and 4-nitro isomers are the same, the supramolecular structures of these isomers are, respectively, three-dimensional and two-dimensional.

Intrigued by the structural variations within series (H)–(K), with respect to both the nature of the aryl substituent and of its location, we subsequently investigated the influence of both variables within the series of *N*-isonicotinoyl arylaldehyde hydrazones (*L*) (Wardell *et al.*, 2007*b*). Here we were able to undertake a genuine two-dimensional study including not only the unsubstituted parent compound having R = H, but the complete sets of 2-, 3- and 4-substituted geometric isomers for each of the series with R = F, Br and OMe, and two of the three-geometric isomers for each of R = Cl and OEt. In total, eight different types of hydrogen bond were found in this series of structures along with $\pi\cdots\pi$ stacking interactions, and the supramolecular structures exhibit a very wide range of combinations of intermolecular interactions. The resulting

hydrogen-bonded structures range from one-dimensional to three-dimensional, often with a different dimensionality for each geometric isomer formed by a particular aryl substituent. We have now followed up this two-dimensional study with a further closely related series of structures in which we have once again varied both the nature and the location of the substituent within the aryl ring.

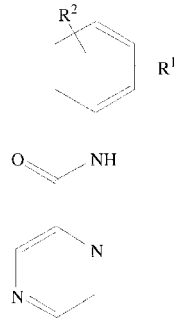


(I) R = H
(II) R = 2-Me, (III) R = 3-Me, (IV) R = 4-Me
(V) R = 2-CF_3, (VI) R = 3CF_3, (VII) R = 4CF_3
(VIII) R = 2-F, (IX) R = 3-F, (X) R = 4-F
(XI) R = 2-Cl, (XII) R = 3-Cl, (XIII) R = 4-Cl
(XIV) R = 2-OMe, (XV)* R = 3-OMe, (XVI) R = 4-OM
(XVII) R = 2NO_2, (XVIII) R = 3NO_2, (XIX) R = 4-NO_2

* (XV) crystallises as a stoichiometric monohydrate

Scheme 2

As a part of this study we have also investigated a selected number of examples with two such substituents.



(XX) R^1 = 2-Me, R^2 = 6-Me
(XXI) R^1 = 2-F, R^2 = 6-F
(XXII) R^1 = 2-Cl, R^2 = 4-F
(XXIII) R^1 = 4-Cl, R^2 = 2-F
(XXIV) R^1 = 2-Me, R^2 = 5-NO_2

Scheme 3

An important aspect of all these structures is the nature of the hetero-aromatic ring, this time a pyrazine ring, where the presence of the proximal N atom has a profound effect upon the hydrogen-bonded supramolecular structures, which range from finite zero-dimensional structures in (V) and (XX), *via* hydrogen-bonded chains in (I), VII), (X), (XIII) and (XXII), and chains of rings in (III), (XII) and (XXI), to hydrogen-bonded sheets in (XVII), and (XXIV).

2. Experimental

2.1. Synthesis

2-Pyrazinecarbonyl chloride was prepared by reacting pyrazinecarboxylic acid with a threefold molar excess of thionyl chloride in dichloromethane solution at ambient temperature with continuous stirring under a dinitrogen atmosphere in the presence of 0.1 equivalents of *N*,*N*-dimethylformamide. After 3 h, the excess thionyl chloride and the other volatiles were removed under reduced pressure to leave the acyl chloride, which was used without purification in the next stage.

A solution of 2-pyrazinecarbonyl chloride (2.4 mmol), as prepared above, and the appropriate substituted aniline (2.0 mmol) in tetrahydrofuran (30 cm^3) was stirred at ambient temperature, for periods between 4 and 12 h depending upon the rate of reaction as monitored by thin-layer chromatography. The reaction mixtures were then cooled and the solvent was removed under reduced pressure. Saturated aqueous sodium hydrogencarbonate solution was added to the residue, and the resulting mixture was exhaustively extracted with ethyl acetate. The combined organic fractions were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The resulting solids were purified either by column chromatography on silica gel, eluting with hexane changing stepwise up to 20% v/v ethyl acetate in hexane, or by successive washings with cold ethanol and diethyl ether, and finally recrystallized from ethanol, to give the products as follows: (I) m.p. 393–394 K [lit. m.p. (McKenzie & Foye, 1972) 396–398 K]; (II) m.p. 383–384 K [lit. m.p. (McKenzie & Foye, 1972) 386–387 K]; (III) m.p. 386–388 K; (IV) m.p. 422–424 K [lit. m.p. (Stanovnik *et al.*, 1980) 423–424 K]; (V) 399–401 K; (VII) 414–416 K; (X) m.p. 425–426 K; (XI) m.p. 407–409 K [lit. m.p. (Kushner *et al.*, 1952) 408–409 K]; (XII) m.p. 415–418 K [lit. m.p. (Kushner *et al.*, 1952) 418–420 K]; (XIII) m.p. 455–457 K [lit. m.p. (Kushner *et al.*, 1952) 457–458 K]; (XIV) m.p. 391–393 K; (XV) m.p. 388–391 K; (XVII) m.p. 443–445 K; (XVIII) m.p. 446–447 K; (XIX) m.p. 496–498 K; (XX) m.p. 380–382 K [lit. m.p. (McKenzie & Foye, 1972) 383–385 K]; (XXI) m.p. 395–396 K; (XXII) m.p. 403–405 K; (XXIII) and (XXIV) m.p. 438–439 K. Crystals suitable for single-crystal X-ray diffraction were obtained for (I)–(V), (VII), (X) in two polymorphic forms (X*a*) and (X*b*), (XI)–(XV), and (XVII)–(XXIV). When a sample of (X) was crystallized from ethanol in an air-conditioned laboratory in San Antonio, Texas, polymorph (X*a*) was obtained, but the same procedure in a non-air-conditioned laboratory in Rio de Janeiro gave polymorph (X*b*). However, despite considerable effort, no homogeneous materials corresponding to (VI), (VIII), (IX) and (XVI) were obtained. Although (XI), (XVIII) and (XIX) were all synthesized in a satisfactory manner, crystals of adequate quality could not be obtained for (XI) and (XVIII), while no diffraction data amenable to structure solution were obtained for (XIX).

2.2. Data collection, structure solution and refinement

Data for (XXII) were collected at 120 (2) K on Daresbury SRS station 9.8 (Cernik *et al.*, 1997; Clegg, 2000) using a Bruker SMART APEX-II diffractometer and synchrotron radiation (λ = 0.6709 Å). Diffraction data for all other compounds were collected at 120 (2) K using a Nonius Kappa-

Table 1
Experimental details.

	(I)	(II)	(III)	(IV)	(V)
Crystal data					
Chemical formula	$C_{11}H_9N_3O$	$C_{12}H_{11}N_3O$	$C_{12}H_{11}N_3O$	$C_{12}H_{11}N_3O$	$C_{12}H_8F_3N_3O$
M_r	199.21	213.24	213.24	213.24	267.21
Cell setting, space group	Triclinic, $P\overline{1}$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Triclinic, $P\overline{1}$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)	120 (2)
a, b, c (Å)	5.9716 (3), 7.5270 (4), 11.0318 (6)	15.5361 (9), 7.0360 (3), 18.9863 (9)	10.2736 (4), 10.8639 (4), 18.5040 (5)	14.0039 (3), 5.6916 (2), 13.3466 (3)	7.6748 (3), 7.8967 (3), 9.8421 (5)
α, β, γ (°)	83.295 (3), 85.377 (4), 69.009 (3)	90.00, 91.307 (2), 90.00	90.00, 90.1970 (19), 90.00	90.00, 101.6381 (12), 90.00	96.682 (2), 103.357 (3), 101.659 (2)
V (Å^3)	459.38 (4)	2074.89 (18)	2065.24 (12)	1041.92 (5)	559.99 (4)
Z	2	8	8	4	2
D_x (Mg m^{-3})	1.440	1.365	1.372	1.359	1.585
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.10	0.09	0.09	0.09	0.14
Crystal form, colour	Plate, colourless	Needle, colourless	Lath, colourless	Block, colourless	Plate, colourless
Crystal size (mm)	0.28 × 0.22 × 0.02	0.52 × 0.04 × 0.02	0.28 × 0.10 × 0.06	0.45 × 0.20 × 0.20	0.24 × 0.20 × 0.06
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}	0.978	0.965	0.979	0.963	0.974
T_{max}	0.998	0.998	0.995	0.982	0.992
No. of measured, independent and observed reflections	7558, 2101, 1823	25 597, 4787, 2575	17 301, 4681, 3543	16 571, 2386, 2047	11 305, 2568, 1916
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}	0.039	0.112	0.051	0.032	0.047
θ_{max} (°)	27.6	27.7	27.5	27.5	27.6
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, 0.119, 1.05	0.110, 0.160, 1.08	0.049, 0.132, 1.05	0.041, 0.122, 1.04	0.047, 0.129, 1.07
No. of reflections	2101	4787	4681	2386	2568
No. of parameters	136	292	291	146	172
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	$w = 1/[\sigma^2(F_o^2) + (0.0433P)^2 + 0.265P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0378P)^2 + 1.5066P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0516P)^2 + 1.1453P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.072P)^2 + 0.2478P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0619P)^2 + 0.1239P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.0001	< 0.0001	0.004	< 0.0001	< 0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.31, −0.23	0.26, −0.22	0.26, −0.33	0.26, −0.21	0.24, −0.31
Extinction method	None	*SHELXL*	None	None	None
Extinction coefficient	–	0.0022 (5)	–	–	–

	(VII)	(X*a*)	(X*b*)	(XII)	(XIII)
Crystal data					
Chemical formula	$C_{12}H_8F_3N_3O$	$C_{11}H_8FN_3O$	$C_{11}H_8FN_3O$	$C_{11}H_8ClN_3O$	$C_{11}H_8ClN_3O$
M_r	267.21	217.20	217.20	233.65	233.65
Cell setting, space group	Triclinic, $P\overline{1}$	Monoclinic, $P2_1/c$	Monoclinic, Pc	Monoclinic, $P2_1/n$	Triclinic, $P\overline{1}$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)	120 (2)
a, b, c (Å)	5.8885 (6), 7.5257 (9), 13.2762 (16)	11.718 (2), 5.9726 (10), 13.474 (2)	5.9666 (3), 24.2205 (15), 13.0262 (7)	9.9121 (3), 10.9457 (3), 18.6827 (4)	5.8636 (3), 7.243 (5), 13.1459 (9)
α, β, γ (°)	78.349 (7), 86.460 (8), 70.146 (8)	90.00, 91.446 (9), 90.00	90.00, 91.720 (3), 90.00	90.00, 92.026 (2), 90.00	100.854 (3), 97.750 (4), 110.783 (4)
V (Å^3)	541.95 (11)	942.7 (3)	1881.62 (18)	2025.71 (9)	500.14 (6)
Z	2	4	8	8	2
D_x (Mg m^{-3})	1.637	1.530	1.533	1.532	1.552
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.14	0.12	0.12	0.36	0.36
Crystal form, colour	Plate, colourless	Needle, colourless	Lath, colourless	Block, colourless	Lath, colourless
Crystal size (mm)	0.62 × 0.36 × 0.06	0.46 × 0.09 × 0.04	0.18 × 0.11 × 0.05	0.56 × 0.38 × 0.14	0.26 × 0.05 × 0.02

Table 1 (continued)

	(VII)	(X*a*)	(X*b*)	(XII)	(XIII)
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}	0.923	0.958	0.966	0.826	0.944
T_{max}	0.991	0.995	0.994	0.952	0.993
No. of measured, independent and observed reflections	11 286, 2499, 1693	9806, 2161, 1031	16 896, 4277, 3351	24 690, 4631, 3461	10 153, 2307, 1780
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}	0.057	0.135	0.052	0.045	0.076
θ_{max} (°)	27.6	27.6	27.5	28.5	27.7
Refinement					
Refinement on	F^2	F^2	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.057, 0.167, 1.01	0.081, 0.225, 1.03	0.045, 0.111, 1.05	0.036, 0.093, 1.04	0.042, 0.102, 1.04
No. of reflections	2499	2161	4277	4631	2307
No. of parameters	172	145	577	289	145
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	$w = 1/[\sigma^2(F_o^2) + (0.1116P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.103P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0412P)^2 + 0.8298P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0476P)^2 + 0.3443P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0384P)^2 + 0.2405P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.0001	< 0.0001	< 0.0001	0.001	0.001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.32, −0.48	0.29, −0.36	0.24, −0.24	0.25, −0.38	0.27, −0.30
Extinction method	None	None	None	None	None

	(XIV)	(XV)	(XVII)	(XX)	(XXI)
Crystal data					
Chemical formula	$C_{12}H_{11}N_3O_2$	$C_{12}H_{11}N_3O_2.H_2O$	$C_{11}H_8N_4O_3$	$C_{13}H_{13}N_3O$	$C_{11}H_7F_2N_3O$
M_r	229.24	247.25	244.21	227.26	235.20
Cell setting, space group	Orthorhombic, *Pbca*	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $C2/c$
Temperature (K)	120 (2)	120 (2)	120 (2)	120 (2)	120 (2)
a, *b*, *c* (Å)	14.1667 (4), 20.7513 (6), 7.4516 (3)	6.9386 (2), 8.5820 (3), 19.0670 (6)	3.6598 (2), 21.7123 (17), 13.1158 (10)	7.3977 (4), 10.7671 (5), 15.2457 (4)	9.8054 (4), 10.9355 (5), 19.4805 (9)
β (°)	90.00	99.394 (2)	91.281 (5)	101.665 (3)	103.474 (2)
V (Å^3)	2190.60 (12)	1120.16 (6)	1041.96 (13)	1189.27 (9)	2031.34 (16)
Z	8	4	4	4	8
D_x (Mg m^{-3})	1.390	1.466	1.557	1.269	1.538
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.10	0.11	0.12	0.08	0.13
Crystal form, colour	Lath, colourless	Needle, orange	Lath, yellow	Plate, colourless	Plate, colourless
Crystal size (mm)	0.38 × 0.36 × 0.10	0.48 × 0.08 × 0.06	0.26 × 0.04 × 0.02	0.48 × 0.16 × 0.05	0.20 × 0.14 × 0.03
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}	0.984	0.961	0.980	0.975	0.984
T_{max}	0.990	0.994	0.997	0.996	0.996
No. of measured, independent and observed reflections	16 739, 2509, 1862	14 126, 2566, 2132	12 339, 2341, 1418	16 731, 2723, 1775	12 350, 2312, 1768
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}	0.046	0.050	0.116	0.061	0.059
θ_{max} (°)	27.5	27.6	27.3	27.5	27.4
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, 0.099, 1.05	0.042, 0.109, 1.05	0.060, 0.140, 1.05	0.047, 0.120, 1.05	0.043, 0.109, 1.03
No. of reflections	2509	2566	2341	2723	2312
No. of parameters	155	164	164	156	154

Table 1 (continued)

	(XIV)	(XV)	(XVII)	(XX)	(XXI)
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	$w = 1/[\sigma^2(F_o^2) + (0.0506P)^2 + 0.185P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.044P)^2 + 0.5866P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0568P)^2 + 0.1342P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0584P)^2 + 0.0716P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0472P)^2 + 1.574P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.17, −0.24	0.28, −0.25	0.28, −0.26	0.16, −0.28	0.19, −0.24
Extinction method	None	None	*SHELXL*	None	None
Extinction coefficient	–	–	0.013 (3)	–	–

	(XXII)	(XXIII)	(XXIV)
Crystal data			
Chemical formula	$C_{11}H_7ClFN_3O$	$C_{11}H_7ClFN_3O$	$C_{12}H_{10}N_4O_3$
M_r	251.65	251.65	258.24
Cell setting, space group	Monoclinic, *Cc*	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	120 (2)	120 (2)	120 (2)
a, *b*, *c* (Å)	18.733 (4), 3.8502 (8), 14.839 (3)	6.8885 (2), 10.5369 (5), 14.6683 (7)	10.4767 (5), 14.5930 (6), 7.7136 (3)
β (°)	99.472 (3)	99.008 (3)	93.433 (3)
V (Å^3)	1055.7 (4)	1051.54 (8)	1177.19 (9)
Z	4	4	4
D_x (Mg m^{-3})	1.583	1.590	1.457
Radiation type	Synchrotron	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.36	0.36	0.11
Crystal form, colour	Block, colourless	Needle, colourless	Plate, colourless
Crystal size (mm)	0.07 × 0.05 × 0.03	0.48 × 0.08 × 0.06	0.34 × 0.04 × 0.02
Data collection			
Diffractometer	Bruker SMART APEXII CCD	Bruker–Nonius KappaCCD	Bruker–Nonius KappaCCD
Data collection method	Fine–slice ω scans	φ and ω scans	φ and ω scans
Absorption correction	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.975	0.845	0.977
T_{max}	0.989	0.979	0.998
No. of measured, independent and observed reflections	5237, 2980, 2888	14 068, 2414, 1903	26 700, 2711, 1936
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.017	0.088	0.094
θ_{max} (°)	28.6	27.6	27.5
Refinement			
Refinement on	F^2	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.034, 0.091, 1.07	0.054, 0.136, 1.07	0.058, 0.153, 1.10
No. of reflections	2980	2414	2711
No. of parameters	154	154	173
H-atom treatment	Constrained to parent site	Constrained to parent site	Constrained to parent site
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0682P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0594P)^2 + 0.780P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0597P)^2 + 0.635P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.0001	< 0.0001	< 0.0001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.51, −0.30	0.41, −0.60	0.31, −0.22
Extinction method	None	None	None
Absolute structure	Flack (1983), 1364 Friedel pairs	–	–
Flack parameter	0.16 (4)	–	–

Computer programs used: *COLLECT* (Hooft, 1999), *DENZO* (Otwinowski & Minor, 1997), *OSCAIL* (McArdle, 2003), *SHELXS*97 (Sheldrick, 1997*a*), *SHELXL*97 (Sheldrick, 1997*b*), *PLATON* (Spek, 2003), *PRPKAPPA* (Ferguson, 1999), *APEX*2 (Bruker AXS, 2003), *SAINT* (Bruker, 2001), *SADABS* (Sheldrick, 2003).

CCD diffractometer, and in all these cases graphite-monochromated Mo $K\alpha$ radiation (λ = 0.71073 Å) was employed. Other details of cell data, data collection and refinement are summarized in Table 1, together with details of the software employed.

For (II), (IV), (X*a*), (XV), (XX), XXIII) and (XXIV) the space group $P2_1/c$ was uniquely assigned from the systematic absences; similarly, the space group $P2_1/n$ was established for (III) and (XVII), and the space group *Pbca* was established for (XIV). Crystals of (V), (VI) and (XIII) are triclinic and for each the space group $P\bar{1}$ was selected, and subsequently confirmed by the successful structure analysis. For each of compounds (XXI) and (XXII), the systematic absences permitted *Cc* or *C*2/*c* as possible space groups: *Cc* was selected for (XXII) and *C*2/*c* was selected for (XXI), and both choices were confirmed by the subsequent structure analyses. Simi-

Table 2
Selected torsional angles (°).

	C*x*2—C*x*7—N*x*17—C*x*11	N*x*17—C*x*7—C*x*2—N*x*1	C*x*7—N*x*17—C*x*11—C*x*12
(I)			
x = nil	−179.67 (12)	1.23 (19)	−11.7 (2)
(II)			
x = 1	176.0 (2)	−2.9 (4)	−146.2 (3)
x = 2	−176.4 (3)	0.5 (4)	152.1 (3)
(III)			
x = 1	179.60 (14)	5.2 (2)	−30.1 (2)
x = 2	−177.52 (15)	4.2 (2)	−10.9 (3)
(IV)			
x = nil	−178.26 (9)	−8.83 (15)	−34.23 (17)
(V)			
x = nil	178.20 (15)	2.4 (2)	171.11 (15)
(VII)			
x = nil	−179.95 (17)	−2.1 (3)	13.9 (3)
(X*a*)			
x = nil	179.4 (3)	−2.2 (5)	−7.9 (6)
(X*b*)			
x = 1	−179.4 (3)	1.0 (5)	11.2 (6)
x = 2	178.2 (3)	0.0 (5)	−14.1 (6)
x = 3	178.2 (3)	−2.8 (5)	13.7 (6)
x = 4	−179.9 (3)	1.5 (5)	−10.9 (6)
(XII)			
x = 1	178.55 (15)	4.1 (2)	−29.5 (2)
x = 2	−179.46 (15)	3.0 (2)	−9.5 (3)
(XIII)			
x = nil	−179.78 (16)	−0.5 (2)	−169.58 (17)
(XIV)			
x = nil	176.63 (11)	−2.27 (15)	−172.77 (12)
(XV)			
x = nil	−178.37 (12)	13.01 (18)	−12.4 (2)
(XVII)			
x = nil	179.4 (2)	7.6 (3)	169.2 (2)
(XX)			
x = nil	179.51 (13)	−4.62 (19)	68.1 (2)
(XXI)			
x = nil	−174.78 (13)	−5.2 (2)	−58.2 (2)
(XXII)			
x = nil	−175.85 (13)	−0.47 (19)	−178.63 (14)
(XXIII)			
x = nil	178.13 (18)	−3.3 (3)	−173.3 (2)
(XXIV)			
x = nil	−178.6 (2)	−5.6 (3)	179.4 (2)

larly, the space group *Pc* was selected and confirmed for (X*b*): a search for possible additional symmetry in (X*b*) revealed none.

The structures were solved by direct methods and refined with all data on F^2. 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 from difference maps and then treated as riding atoms with C—H distances of 0.95 Å (aromatic) or 0.98 Å (methyl) and N—H distances of 0.88 Å, and with $U_{iso}(H) = 1.2U_{eq}(C,N)$ or $1.5U_{eq}(C)$ for the methyl groups. For (XXII) the correct orientation of the structure with respect to the polar axis directions was established by means of the Flack parameter (Flack, 1983). For (X*b*), the absence of significant resonant scattering meant that the correct orientation of the structure with respect to the polar axis directions could not be established: hence the Friedel-equivalent reflections were merged prior to the final refinements.

Supramolecular analyses were made and the diagrams were prepared with the aid of *PLATON* (Spek, 2003). Details of molecular conformations are given in Table 2, and details of hydrogen-bond dimensions are given in Table 3. Fig. 1 shows the molecular structures of representative examples, selected to illustrate the atom-labelling schemes; Figs. 2–7 show aspects of the supramolecular structures.[1]

3. Results and discussion

3.1. Crystallization characteristics

Of the compounds investigated here, only one, the 4-fluorophenyl compound (X), has been found in polymorphic forms: a $Z' = 1$ polymorph in space group $P2_1/c$, compound (X*a*) and a $Z' = 4$ polymorph in space group *Pc*, compound (X*b*). Both polymorphs were obtained by crystallization from ethanol solution; polymorph (X*a*) was obtained in San Antonio, Texas, while polymorph (X*b*) was obtained in Rio de Janeiro, although to the best of our knowledge, this compound had not previously been crystallized in either location. The densities of the two polymorphs are very similar, 1.530 g cm^{-3} for (X*a*) and 1.533 g cm^{-3} for (X*b*), such that deductions about their relative thermodynamic stability cannot plausibly be made (Burger & Ramberger, 1979). Possible interpretations of this behaviour include a dependency on the exact water content of the ethanol employed as the crystallization solvent, as this is likely to have been higher in the humid climate of Rio de Janeiro than in the air-conditioned laboratory environment in San Antonio; or concomitant crystallization (Bernstein *et al.*, 1999), with crystals of different polymorphs being selected from the two crystallizations by chance. We emphasize, however, that we have not at this time investigated the polymorphism of (X) further.

Only a single pair of compounds, the 3-methylphenyl compound (III) and the 3-chlorophenyl compound (XII), have been found to be isomorphous and effectively isostructural: this pair both crystallize with $Z' = 2$ in the space group $P2_1/n$: by contrast, the corresponding pair of 4-substituted isomers, (IV) and (XIII), adopt entirely different supramolecular structures, in space groups $P2_1/c$ and $P\bar{1}$, respectively. Apart from the 2-methylphenyl derivative (II), which crystallizes with $Z' = 2$ in the space group $P2_1/c$, and those noted above all other compounds in this study crystallize with $Z' = 1$.

Three compounds of the $Z' = 1$ type, (I), (V) and (VII), crystallize in the space group $P\bar{1}$, while seven compounds, (IV), (X*a*), (XV), (XVII), (XX), (XXIII) and (XXIV), crys-

[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM5049). Services for accessing these data are described at the back of the journal.

tallize in $P2_1/c$ or $P2_1/n$, and one each in Cc, $C2/c$ and $Pbca$, (XXII), (XXI) and (XIV), respectively. The compounds having $Z' = 2$, (II), (III) and (XII), all crystallize in $P2_1/c$ or $P2_1/n$, and the sole example with $Z' = 4$, compound (X*b*), crystallizes in Pc. Hence, even within this quite compact series of related amides, the predominance of $P2_1/c$ and $P2_1/n$ is already evident.

The 3-methoxyphenyl compound (XV) is the only solvated form observed during the course of this study: it crystallizes from ethanol as a stoichiometric monohydrate.

3.2. Molecular conformations

The molecular conformations (Fig. 1) are, in general, defined by just three torsional angles (Table 2). In all cases the central amide unit adopts the usual *trans* planar conformation, and the pyrazine ring is effectively coplanar with the amide unit and oriented such that the amido N—H unit makes a short intramolecular contact with one of the pyrazine ring N atoms (Table 3) forming an $S(5)$ motif (Bernstein *et al.*, 1995). This attractive contact can be regarded as the intramolecular hydrogen bond responsible for the coplanarity of the pyrazine rings with the amido spacer units.

However, the orientation of the substituted aryl rings varies quite markedly. For the compounds which crystallize with $Z' = 1$, the aryl ring is nearly coplanar with the rest of the molecule in (V), (XIII), (XIV), (XVII), (XXII) and (XXIV), but the aryl ring is nearly orthogonal to the rest of the molecule in both (XX) and (XXI), where the aryl ring carries substituents at both the 2- and the 6-positions. It can be concluded that the rotation of the aryl ring about the N17—C11 bond in (XX) and (XXI) is driven by a repulsive interaction between a ring substituent and the amidic O atom.

For (II), (III) and (XII), which crystallize with $Z' = 2$, the conformations indicate that the two molecules in the selected asymmetric unit of (II) are very close to being enantiomorphs, although this is not the case in the isostructural pair (III) and (XII), where the torsional angles about the bonds N27—C21 and N47—C41 differ by almost 20°. The conformations in (II) and (III) also differ markedly in the location of the pendent methyl groups, adjacent to the N—H bond in (II) and remote from it in (III) (Figs. 1*a* and *b*).

The four independent molecules of (X*b*) all adopt very similar conformations. Within the asymmetric unit as specified, the molecules of types 1 and 3 are effectively enantiomeric with the molecules of types 2 and 4 (Table 2): however, the space group Pc ensures that equal numbers of the

Table 3
Parameters (Å, °) for hydrogen bonds and short intramolecular contacts.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*	Motif	Direction
(I)						
N17—H17···N1	0.90	2.31	2.7050 (17)	107	*S*(5)	–
C16—H16···O7^{i}	0.95	2.37	3.220 (2)	148	*C*(6)	[100]
(II)						
N117—H117···N11	0.88	2.16	2.655 (3)	115	*S*(5)	–
N217—H217···N31	0.88	2.18	2.654 (3)	113	*S*(5)	–
(III)						
N117—H117···N11	0.88	2.30	2.730 (2)	110	*S*(5)	–
N217—H217···N21	0.88	2.31	2.736 (2)	110	*S*(5)	–
N117—H117···N24^{ii}	0.88	2.46	3.271 (2)	153	*D*†	–
N217—H217···N14	0.88	2.45	3.278 (2)	157	*D*†	–
C23—H23···N11^{iii}	0.95	2.59	3.245 (2)	126	*D*†	–
C216—H216···N14	0.95	2.61	3.393 (2)	140	*D*†	–
(IV)						
N17—H17···N1	0.96	2.26	2.7265 (14)	108	*S*(5)	–
C5—H5···N4^{iv}	0.95	2.51	3.3803 (15)	152	*C*(3)	[010]
C16—H16···O7^{ii}	0.95	2.43	3.2617 (15)	146	*C*(6)	[010]
(V)						
N17—H17···N1	0.92	2.11	2.6770 (19)	119	*S*(5)	–
C15—H15···O7^{v}	0.95	2.46	3.365 (2)	159	$R_2^2(14)$	–
(VII)						
N17—H17···N1	0.88	2.29	2.719 (2)	110	*S*(5)	–
C16—H16···O7^{i}	0.95	2.36	3.174 (2)	143	*C*(6)	[100]
(X*a*)						
N17—H17···N1	0.99	2.11	2.700 (4)	117	*S*(5)	–
C16—H16···O7^{ii}	0.95	2.43	3.271 (4)	147	*C*(6)	[010]
(X*b*)						
N117—H117···N11	0.88	2.26	2.702 (4)	111	*S*(5)	–
N217—H217···N21	0.88	2.22	2.709 (4)	115	*S*(5)	–
N317—H317···N31	0.88	2.27	2.700 (4)	110	*S*(5)	–
N417—H417···N41	0.88	2.19	2.693 (5)	116	*S*(5)	–
C116—H116···O17^{vi}	0.95	2.45	3.279 (5)	146	*C*(6)	[100]
C216—H216···O27^{i}	0.95	2.44	3.290 (5)	148	*C*(6)	[100]
C316—H316···O37^{vi}	0.95	2.36	3.232 (5)	152	*C*(6)	[100]
C416—H416···O47^{i}	0.95	2.42	3.257 (5)	147	*C*(6)	[100]
(XII)						
N117—H117···N11	0.87	2.24	2.6339 (19)	108	*S*(5)	–
N217—H217···N21	0.87	2.24	2.6368 (18)	108	*S*(5)	–
N117—H117···N24^{ii}	0.87	2.43	3.2248 (19)	153	*D*†	–
N217—H217···N14	0.87	2.48	3.2954 (19)	156	*D*†	–
C23—H23···N11^{iii}	0.95	2.54	3.321 (2)	129	*D*†	–
C216—H216···N14	0.95	2.52	3.302 (2)	140	*D*†	–
(XIII)						
N17—H17···N1	0.88	2.24	2.718 (2)	114	*S*(5)	–
C16—H16···O7^{i}	0.95	2.38	3.176 (3)	141	*C*(6)	[100]
(XIV)						
N17—H17···N1	0.88	2.15	2.6522 (15)	115	*S*(5)	–
C6—H6···O7^{vii}	0.95	2.39	3.1389 (16)	136	*C*(6)	[100]
(XV)						
N17—H17···N1	0.88	2.31	2.7283 (16)	109	*S*(5)	–
N17—H17···O1	0.88	2.25	3.0105 (15)	145	*D*	–
O1—H1*A*···N4^{iii}	0.90	2.00	2.8947 (16)	173	*D*‡	–
O1—H1*B*···O7^{viii}	0.90	1.93	2.8092 (15)	165	*D*§	–
(XVII)						
N17—H17···N1	0.88	2.27	2.686 (3)	109	*S*(5)	–
N17—H17···O121	0.88	1.94	2.649 (3)	137	*S*(6)	–
C14—H14···O122^{ix}	0.95	2.54	3.422 (3)	155	*C*(6)	[10$\bar{1}$]
C15—H15···O7^{viii}	0.95	2.52	3.257 (3)	134	$R_2^2(14)$	–
(XX)						
N17—H17···N1	0.88	2.20	2.6518 (16)	111	*S*(5)	–
C3—H3···O7^{viii}	0.95	2.41	3.2688 (18)	150	$R_2^2(10)$	–
(XXI)						
N17—H17···N1	0.88	2.36	2.7280 (19)	105	*S*(5)	–
N17—H17···N4^{x}	0.88	2.29	3.1230 (19)	157	*C*(6)	[010]
C3—H3···N1^{xi}	0.95	2.48	3.208 (2)	134	*C*(4)	[010]
(XXII)						
N17—H17···N1	0.88	2.21	2.674 (2)	113	*S*(5)	–
C13—H13···N4^{xii}	0.95	2.43	3.364 (2)	170	*C*(9)	[130]
(XXIII)						
N17—H17···N1	0.89	2.14	2.652 (3)	116	*S*(5)	–
(XXIV)						

Table 3 (continued)

D—H···A	D—H	H···A	D···A	D—H···A	Motif	Direction
N17—H17···N1	0.88	2.09	2.630 (2)	119	$S(5)$	–
C6—H6···O151^{xiii}	0.95	2.48	3.373 (3)	156	$C(11)$	[101]
C14—H14···O7^{xiv}	0.95	2.54	3.228 (3)	130	$C(8)$	[010]

Symmetry codes: (i) $-1+x, y, z$; (ii) $x, -1+y, z$; (iii) $x, 1+y, z$; (iv) $-x, -\frac{1}{2}+y, \frac{3}{2}-z$; (v) $-x, -y, 1-z$; (vi) $1+x, y, z$; (vii) $\frac{1}{2}+x, y, \frac{3}{2}-z$; (viii) $1-x, 1-y, 1-z$; (ix) $\frac{1}{2}+x, \frac{1}{2}-y, -\frac{1}{2}+z$; (x) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$; (xi) $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z$; (xii) $-\frac{1}{2}+x, -\frac{3}{2}+y, z$; (xiii) $1+x, y, 1+z$; (xiv) $-x, \frac{1}{2}+y, \frac{1}{2}-z$. † The four independent D motifs combine to generate a $C_2^2(12)C_2^2(12)[R_2^1(6)][R_2^2(8)]$ chain of rings (see text). ‡ The combination of N—H···O and O—H···N hydrogen bonds generates a $C_2^2(8)$ chain parallel to [010] (see text). § The combination of N—H···O and O—H···O hydrogen bonds generates a $R_4^4(12)$ ring (see text).

two enantiomers of each independent molecule are present.

3.3. Supramolecular aggregation

Criticism of the progressive 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···N and C—H···O contacts in which the D—H···A angle is less than 130°;

(ii) C—H···N contacts having the angle C—H···N greater than 130°, but with an H···A distance greater than 2.60 Å;

(iii) a single C—H···O contact in (XXIV), where the C—H bond forms part of a methyl group: not only are such bonds of low acidity but sixfold barriers to intramolecular rotation, such as those for bonds between methyl groups and aryl rings, are generally very low (Tannenbaum *et al.*, 1956; Naylor & Wilson, 1957); and

(iv) all of the C—H···F contacts in (VII), (X*b*) and (XXII) and the single C—H···Cl contact in (XXII), since it is known (Howard *et al.*, 1996; Brammer *et al.*, 2001) that both F and Cl when bonded to C are extremely weak acceptors, particularly from C—H bonds.

As noted above (§3.2), all of the compounds studied here exhibit an intramolecular N—H···N hydrogen bond with the proximal N atom of the pyrazine as the acceptor. In the hydrated 3-methoxyphenyl compound (XV), this N—H···N interaction can be regarded as one component of a three-centre N—H···(N,O) system in which the water O atom within the selected asymmetric unit acts as the second acceptor. In the 2-nitrophenyl compound (XVII) there is also an intramolecular N—H···O hydrogen bond having one of the nitro O atoms as the acceptor, so forming a three-centre N—H···(O,N) system in which both components are intramolecular.

However, with the single exception of (XV) none of the compounds reported here form intermolecular N—H···O hydrogen bonds. There are intermolecular N—H···N hydrogen bonds present in the isostructural pair of compounds (III) and (XII), and in (XXI). Otherwise, however, the amido N—H bond plays no role in the intermolecular hydrogen bonding, almost as if the presence of the intramolecular N—H···N interaction was in most cases sufficient to completely satisfy the hydrogen-bonding requirements of this N—H unit. Hence, none of the structures discussed here contain an intermolecular N—H···O hydrogen bond having the amido O atom as the acceptor, so the chain-forming $C(4)$ motif, characteristic of carboxamides of this general type (Kashino *et al.*, 1979; Bowes *et al.*, 2003; Glidewell *et al.*, 2003; Kumar *et al.*, 2004; Garden *et al.*, 2005; Cuffini *et al.*, 2006; Wardell *et al.*, 2006) and of sulfonamides in general (Vorontsova, 1966; Cotton & Stokely, 1970; Klug, 1970; Brink & Mattes, 1986; Lightfoot *et al.*, 1993;

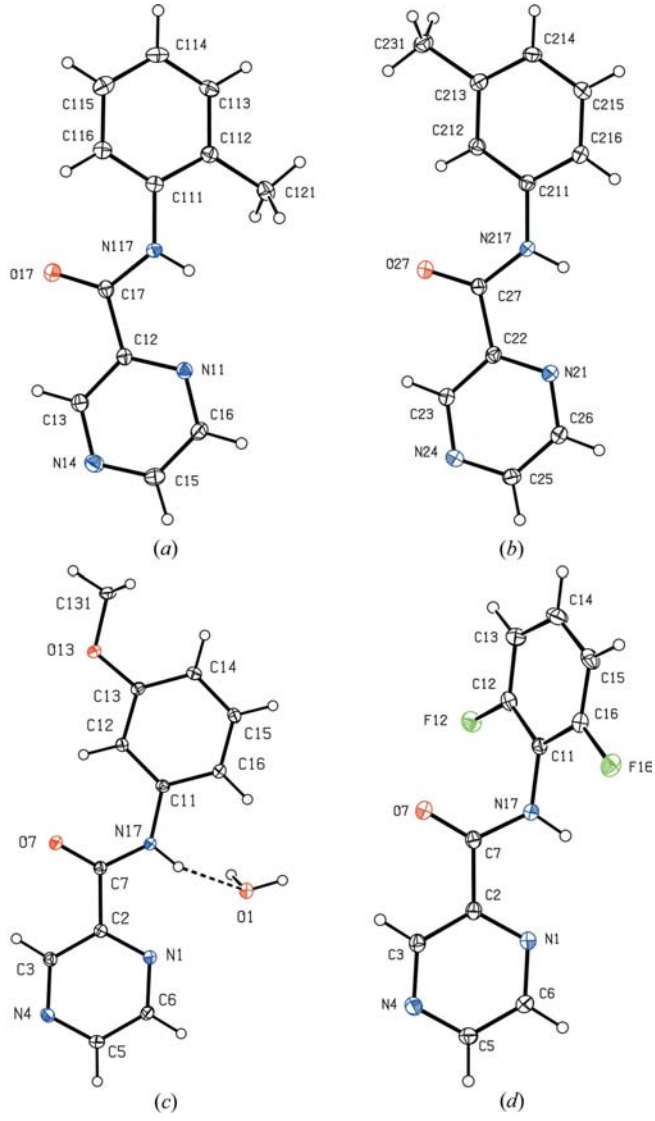


Figure 1
The molecular structures of representative compounds selected to show the atom-labelling schemes and the different molecular conformations: (*a*) type 1 molecule in the 2-methylphenyl compound (II); (*b*) type 2 molecule in the 3-methylphenyl compound (III); (*c*) independent molecular components in the monohydrate of the 3-methoxyphenyl compound (XV); (*d*) molecule of the 2,6-difluorophenyl compound (XXI). In all cases the displacement ellipsoids are drawn at the 30% probability level.

Tremayne *et al.*, 1999, 2002; Kelly *et al.*, 2002; Clark *et al.*, 2003; Wardell *et al.*, 2004), is completely absent from the present series. The supramolecular aggregation for the most part depends upon C—H···O and C—H···N hydrogen bonds (Table 3), and upon $\pi\cdots\pi$ stacking interactions.

3.3.1. Zero-dimensional structures. *Compound (V)*. The supramolecular aggregation of (V) is extremely simple: pairs of molecules are linked by C—H···O hydrogen bonds (Table 3) into centrosymmetric $R_2^2(14)$ (Bernstein *et al.*, 1995) dimers (Fig. 2*a*), but there are no direction-specific interactions between adjacent dimers. Hence, the supramolecular structure can be described as finite or zero-dimensional.

Compound (XX). As in (V), the molecules of (XX) are linked by paired C—H···O hydrogen bonds (Table 3) into centrosymmetric dimers, now of $R_2^2(10)$ type (Fig. 2*b*), but again with no direction-specific interactions between adjacent dimers. It may be noted here that while the hydrogen-bond donor in (V) is a phenyl C atom, in (XX) the donor lies in the pyrazine ring.

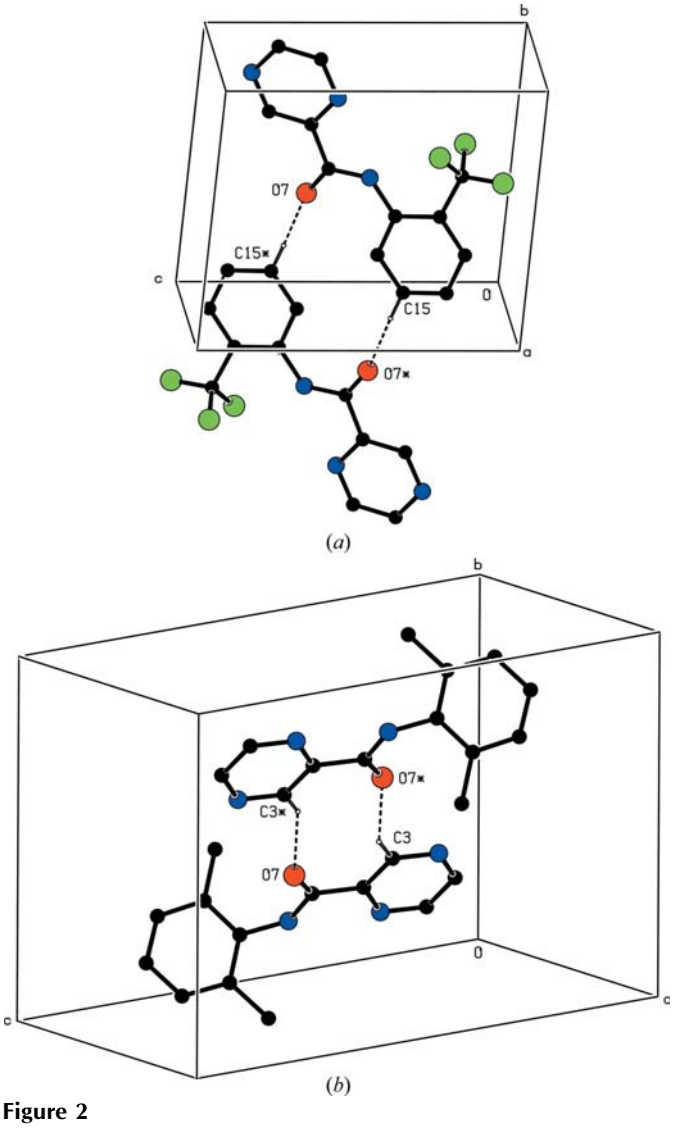


Figure 2
Parts of the crystal structures of (V) and (XX) showing the formation of cyclic centrosymmetric dimers: (*a*) the $R_2^2(14)$ dimer in the 2-trifluoromethylphenyl compound (V), where the atoms marked with an asterisk (*) are at the symmetry position $(-x, -y, 1-z)$; (*b*) the $R_2^2(10)$ dimer in the 2,6-dimethylphenyl compound (XX), where the atoms marked with an asterisk are at the symmetry position $(1-x, 1-y, 1-z)$. For the sake of clarity, the H atoms not involved in the motifs shown have been omitted.

3.3.2. One-dimensional structures. (*a*) Chains formed by π-stacking:

Compound (II). Intermolecular hydrogen bonds of all types are absent from the structure of (II), and the sole direction-specific interactions between the molecules are $\pi\cdots\pi$ stacking interactions, which link the molecules into two distinct chains: one chain contains only molecules of type 1, containing N11, while the other chain contains only molecules of type 2, containing N21. The pyrazine ring of the type 1 molecule at (x, y, z) makes dihedral angles of only 2.5 (2)° with the aryl rings C21–C26 in the type 1 molecules at $(2-x, \frac{1}{2}+y, \frac{1}{2}-z)$ and $(2-x, -\frac{1}{2}+y, \frac{1}{2}-z)$. The ring-centroid separations in these two interactions are 3.675 (2) and 3.617 (2) Å, respectively, with interplanar spacings of *ca* 3.40 and 3.41 Å and ring offsets of *ca* 1.39 and 1.21 Å, respectively. The propagation of these two interactions generates a π-stacked chain running parallel to the [010] direction and generated by the 2_1 screw axis along $(1, y, 0.25)$. In the second chain the pyrazine ring of the type 2 molecule at (x, y, z) makes dihedral angles of 3.8 (2)° with the aryl rings C41–C46 in the type 2 molecules at $(1-x, \frac{1}{2}+y, \frac{1}{2}-z)$ and $(1-x, -\frac{1}{2}+y, \frac{1}{2}-z)$. The ring-centroid separations are 3.660 (2) and 3.622 (2) Å, with interplanar spacings of *ca* 3.48 and 3.38 Å, and ring offsets of 1.13 and 1.30 Å, respectively. Propagation of these two interactions generates a second π-stacked chain, this time running parallel to the [010] direction and generated by the 2_1 screw axis along $(0.5, y, 0.25)$ (Fig. 3*a*). Two chains of each type, related in pairs by inversion, pass through each unit cell, but there are no direction-specific interactions between any of the chains.

Compound (XXIII). In the structure of this compound there are two independent $\pi\cdots\pi$ stacking interactions which combine to link the molecules into chains. The pyrazine ring of the molecule at (x, y, z) is inclined at 2.8 (2)° to the aryl rings of the two molecules at $(1-x, 1-y, 1-z)$ and $(-x, 1-y, 1-z)$: the respective ring-centroid separations are 3.763 (2) and 3.583 (2) Å, with interplanar spacings of *ca* 3.44 and 3.37 Å, corresponding to ring-centroid offsets of *ca* 1.52 and 1.21 Å. The combination of these two interactions generates a π-stacked chain running parallel to the [100] direction (Fig. 3*b*).

(*b*) Simple hydrogen-bonded chains:

Compounds (I), (VII), (Xa), (Xb) and (XIII). In each of compounds (I), (VII), (X*a*) and (XIII), the molecules are linked into $C(6)$ chains by a single C—H···O hydrogen bond, involving in each case the aryl C16 atom as the donor and the carbonyl O atom as the acceptor (Table 3). In the $Z' = 4$ polymorph (X*b*) each of the four independent molecules forms a $C(6)$ chain in exactly the same way as those formed in (I), (VII), (X*a*) and (XIII). In all of these compounds the $C(6)$ chains are generated by translation, and those in (I) (Fig. 4*a*), (VII) and (XIII) run parallel to the [100] direction, while those

in the two polymorphs (X*a*) and(X*b*) all run parallel to the [010] direction. Of the four independent chains in (X*b*), the pairs of chains formed by the molecules of types 1 and 3 run antiparallel to the pair of chains formed by the molecules of types 2 and 4. In each of these compounds, there are no direction-specific interactions between the chains

Compound (XXII). The molecules of (XXII) are linked into simple chains by a single, nearly linear C—H···N hydrogen bond (Table 3). The aryl C13 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor to the ring N4 atom in the molecule at $(-\frac{1}{2}+x, -\frac{3}{2}+y, z)$, so generating by translation a $C(9)$ chain running parallel to the [130] direction (Fig. 4*b*). Two chains of this type, related to one another by the *c*-glide plane, pass through each unit cell but there are no direction-specific interactions between the chains.

(*c*) Hydrogen-bonded chains of rings:

Compounds (III) and (XII). These compounds are isomorphous and effectively isostructural, and hence we discuss the supramolecular aggregation only for (III). Both compounds crystallize with $Z' = 2$ (Fig. 1*b*) and the patterns of the hydrogen bonds (Table 3) suffice to preclude the possibility of any additional crystallographic symmetry. The molecules are linked into chains by two intermolecular N—H···N hydrogen bonds, whose effect is weakly reinforced by two C—H···N hydrogen bonds.

Within the selected asymmetric unit the N217 and C216 atoms both act as hydrogen-bond donors to the N14 atom. In addition, the N117 atom at (x, y, z) acts as a hydrogen-bond donor to the N24 atom at $(x, -1+y, z)$, while the C23 atom at (x, y, z) acts as a donor to the N11 atom at $(x, 1+y, z)$. The two N—H···N hydrogen bonds thus generate by translation a $C_2^2(12)$ chain running parallel to the [010] direction, and the two C—H···N hydrogen bonds similarly form a second $C_2^2(12)$ chain, while the combined action of all these hydrogen bonds generates a chain of alternating $R_2^1(6)$ and $R_2^2(8)$ rings (Fig. 5*a*). Four of these chains of rings pass through each unit cell, but there are no direction-specific interactions between the chains.

Compound (XXI). The molecules of (XXI) are linked into a chain of rings by a combination of two hydrogen bonds, one each of N—H···N and C—H···N types. The atoms N17 and C3 in the molecule at (x, y, z) act as hydrogen-bond donors respectively to ring atoms N4 in the molecule at $(\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z)$ and N1 in the molecule at $(\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z)$, thus forming a $C(4)C(6)[R_2^2(8)]$ chain of rings running parallel to the [010] direction and generated by the 2_1 screw axis along $(0.25, y, 0.25)$ (Fig. 5*b*). Four such chains pass through each unit cell, but there are no direction-specific interactions between the chains.

3.3.3. Two-dimensional structures. (*a*) Sheets of π-stacked hydrogen-bonded chains:

Compound (IV). The ribbon structure of (IV) is built from a combination of one C—H···O hydrogen bond and one C—H···N hydrogen bond (Table 3). The aryl C16 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor to the carbonyl O7 atom in the molecule at $(x, -1+y, z)$, so generating by translation a $C(6)$ chain, entirely analogous to those found in (I), (VII), (X*a*), (X*b*) and (XIII). In addition, however, the pyrazine C5 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor to the pyrazine N4 atom in the molecule at $(-x, -\frac{1}{2}+y, \frac{3}{2}-z)$, so forming a $C(3)$ chain running parallel to the [010] direction and generated by the 2_1 screw axis along $(0, y, 0.75)$. The combination of the $C(3)$ and $C(6)$ motifs generates a ribbon of edge-fused $R_3^3(18)$ rings running parallel to the [010] direction (Fig. 6*a*).

A single $\pi\cdots\pi$ stacking interaction links these ribbons into sheets. The pyrazine rings of the molecules at (x, y, z) and $(-x, 2-y, 1-z)$ are strictly parallel with an interplanar spacing of 3.476 (2) Å and a ring-centroid separation of 3.524 (2) Å. The molecule at $(-x, 2-y, 1-z)$ forms part of the ribbon of edge-fused rings generated by the 2_1 screw axis along $(0, -y, 0.25)$, and propagation of this $\pi\cdots\pi$ stacking interaction by the screw axes links the ribbons into a sheet parallel to (100) and occupying the domain $-0.5 < x < 0.5$. There are no direction-specific interactions between adjacent sheets.

Compound (XIV). In the structure of this compound the molecules are linked into chains by a single C—H···O hydrogen bond, and these chains are linked into sheets by a single $\pi\cdots\pi$ stacking interaction. The chain formation in (XIV) is, once

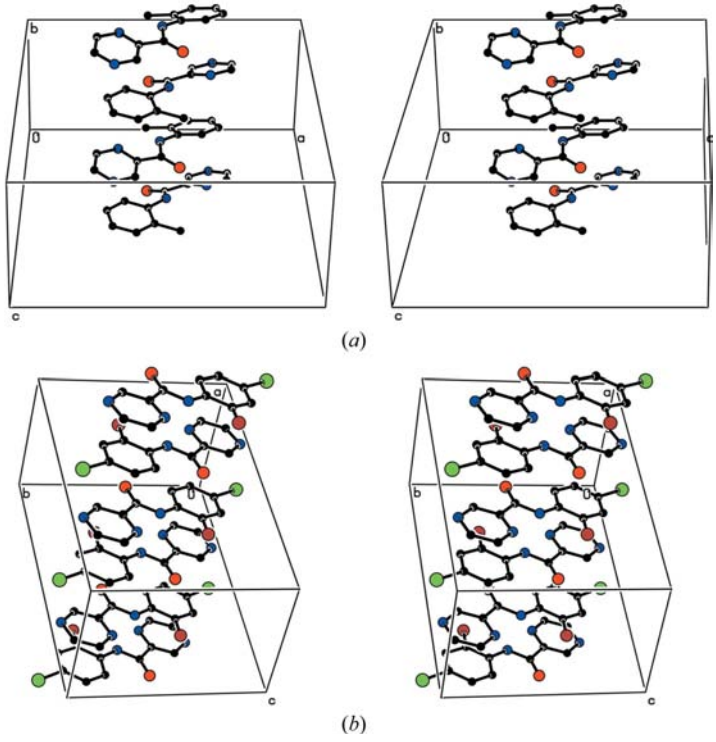


Figure 3
Stereoviews of parts of the crystal structures of (II) and (XXIII), showing the chains formed by π-stacking: (*a*) the chain of type 2 molecules along (0.5, *y*, 0.25) in the 2-methylphenyl compound (II); (*b*) the chain in the 4-chloro-2-fluorophenyl compound (XXIII). For the sake of clarity, the H atoms have all been omitted.

again, based on a single C—H···O hydrogen bond generating a $C(6)$ motif, but in this example only, the hydrogen-bond donor forms part of the pyrazine ring rather than part of the aryl ring, and the chain is generated by a glide plane rather than by translation. The pyrazine C6 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor towards the O7 atom in the molecule at $(\frac{1}{2}+x, y, \frac{3}{2}-z)$, so forming a chain running parallel to the [100] direction and generated by the *a*-glide plane at $z = 0.75$. There are four chains of this type passing through each unit cell, lying in the four domains of y: $0 < y < 0.25$, $0.25 < y < 0.5$, $0.5 < y < 0.75$, and $0.75 < y < 1.0$. Within each of these domains, the chains are linked into sheets by a single $\pi\cdots\pi$ stacking interaction. The pyrazine and aryl rings of the molecules at (x, y, z) and $(x, y, 1+z)$, respectively, make a dihedral angle of only 4.1 (2)°: the ring–centroid separation is 3.691 (2) Å and the interplanar spacing is *ca* 3.36 Å, corresponding to a ring–centroid offset of *ca* 1.52 Å. This interaction links the $C(6)$ chain into sheets parallel to (010), one in each domain of y (Fig. 6*b*), but there are no direction-specific interactions between adjacent sheets.

Compound (XV). Compound (XV) is the sole hydrate amongst the compounds discussed here and the presence of the water component strongly influences the hydrogen-bonding characteristics. The asymmetric unit has been selected such that the two molecular components within it are linked by an N—H···O hydrogen bond (Table 3), and the linkage of these bimolecular aggregates utilizes one O—H···N hydrogen bond and one O—H···O hydrogen bond to generate a chain of edge-fused rings, whose formation is readily analysed in terms of the actions of the two hydrogen bonds, considered first individually and then in combination.

The water atom O1 at (x, y, z) acts as a hydrogen-bond donor, *via* H1*A*, to the pyrazine atom N4 at $(x, 1+y, z)$, so generating by translation a $C_2^2(8)$ chain running parallel to the [010] direction. At the same time, the same O atom acts as a hydrogen-bond donor, *via* H1*B*, to the carbonyl atom O7 at $(1-x, 1-y, 1-z)$, so generating by inversion an $R_4^4(12)$ ring. The combination of these two motifs generates a chain of edge-fused centrosymmetric rings running parallel to the [010] direction, with $R_4^4(12)$ rings centred at $(0.5, n+0.5, 0.5)$ (where n is zero or an integer) alternating with $R_4^4(16)$ rings centred at $(0.5, n, 0.5)$ (where n is zero or an integer) (Fig. 6*c*). Two chains of this type pass through each unit cell, along $(0.5, y, 0.5)$ and $(0.5, y, 0)$, respectively.

There are two independent $\pi\cdots\pi$ stacking interactions in the structure of (XV): one lies within the chain of rings, and the other serves to link these chains into sheets lying in the domains $0.25 < z < 0.75$ and $0.75 < z < 1.25$. The pyrazine and aryl rings of the amide molecules at (x, y, z) and $(-x, 1-y, 1-z)$, respectively, make a dihedral angle of only 1.6 (2)°: the ring-centroid separation is 3.570 (2) Å and the interplanar spacing is *ca* 3.38 Å, corresponding to a ring-centroid offset of *ca* 1.15 Å. The effect of this interaction is to link the chains into sheets parallel to (001), one in each domain of z: there are no direction-specific interactions between these sheets.

(*b*) Hydrogen-bonded sheets:

Compound (XVII). The molecules of (XVII) are linked into sheets by a combination of two C—H···O hydrogen bonds, one of which utilizes the carbonyl O as the acceptor, and the other of which utilizes one of the nitro O atoms as the acceptor (Table 3). The formation of the sheet is readily analysed in terms of the actions of the two individual hydrogen bonds.

The aryl C15 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor to the carbonyl O7 atom in the molecule at $(1-x, 1-y, 1-z)$, so generating by inversion a cyclic centrosymmetric $R_2^2(14)$ dimer centred at (0.5, 0.5, 0.5): this dimeric unit can conveniently be regarded as the basic building block within the sheet.

The C14 atoms in the molecules at (x, y, z) and $(1-x, 1-y, 1-z)$, which form the dimer centred at (0.5, 0.5, 0.5), act as hydrogen-bond donors to the nitro O122 atoms in the molecules at $(\frac{1}{2}+x, \frac{1}{2}-y,$

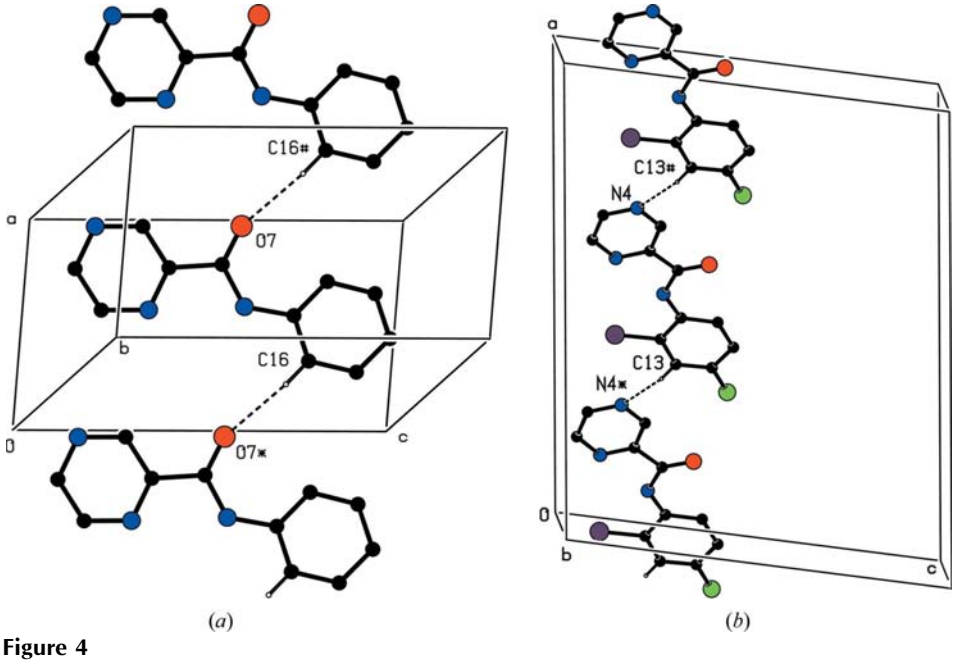


Figure 4
Parts of the crystal structures of (I) and (XXII) showing the formation of simple hydrogen-bonded chains: (*a*) a $C(6)$ chain in the unsubstituted parent compound (I), where the atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(-1+x, y, z)$ and $(1+x, y, z)$, respectively; and (*b*) a $C(9)$ chain in the 2-chloro-4-fluorophenyl compound (XXII), where the atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(-\frac{1}{2}+x, -\frac{3}{2}+y, z)$ and $(\frac{1}{2}+x, \frac{3}{2}+y, z)$, respectively. For the sake of clarity, the H atoms not involved in the motifs shown have been omitted.

$-\frac{1}{2}+z$) and ($\frac{1}{2}-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$), respectively, which themselves form parts of the $R_2^2(14)$ dimers centred at (1, 0, 0) and (0, 1, 1), respectively. Similarly, the O122 atoms at (x, y, z) and ($1-x$, $1-y$, $1-z$) accept hydrogen bonds from the C14 atoms in the molecules at ($\frac{1}{2}+x$, $\frac{3}{2}-y$, $-\frac{1}{2}+z$) and ($\frac{1}{2}-x$, $-\frac{1}{2}+y$, $\frac{3}{2}-z$), respectively, which forms parts of the dimers centred at (1, 1, 0) and (0, 0, 1). Thus, each dimer is linked to four other dimers, and propagation by the space group of these hydrogen bonds generates a sheet lying parallel to (101) and built from centrosymmetric $R_2^2(14)$ and $R_6^6(34)$ rings alternating in a chessboard fashion (Fig. 7*a*): if the $R_2^2(14)$ dimers are regarded as the nodes of the resulting net, then this is of (4,4) type (Batten & Robson, 1998). There are no direction-specific interactions between adjacent sheets.

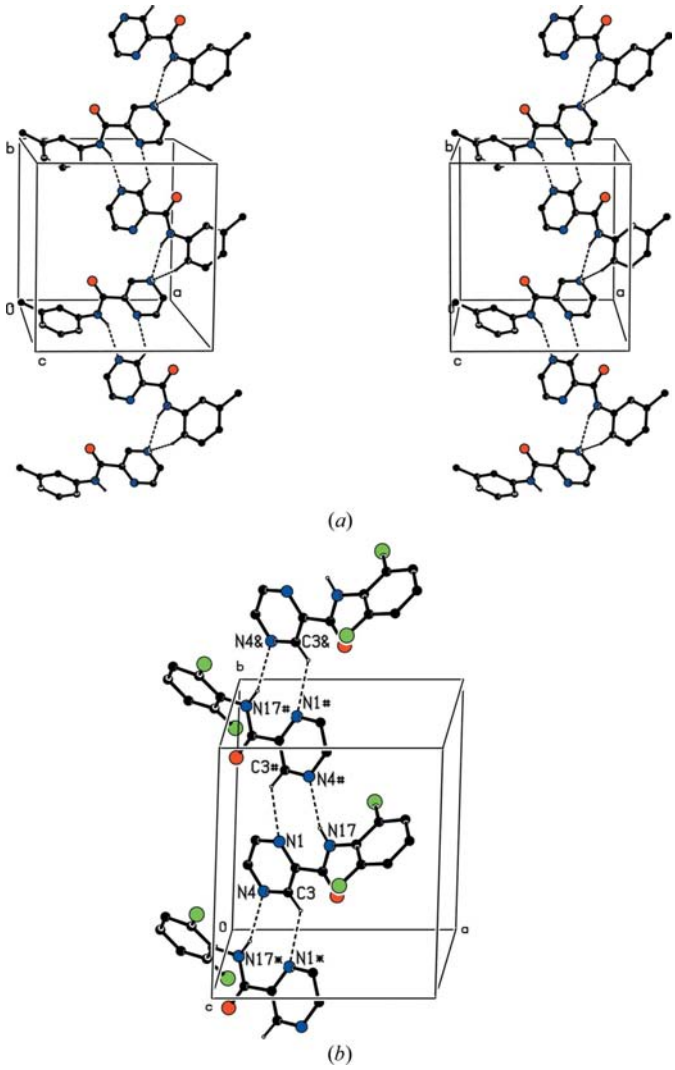


Figure 5
Parts of the crystal structures of (III) and (XXI) showing the formation of simple hydrogen-bonded chains of rings: (*a*) a stereoview of the chain of alternating $R_2^1(6)$ and $R_2^2(8)$ rings in the 3-methylphenyl compound (III); (*b*) the $C(4)C(6)[R_2^2(8)]$ chain of rings in the 2,6-difluorophenyl compound (XXI), where the atoms marked with an asterisk (*), a hash (#) or an ampersand (&) are at the symmetry positions ($\frac{1}{2}-x$, $-\frac{1}{2}+y$, $\frac{1}{2}-z$), ($\frac{1}{2}-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$) and (x, $1+y$, z), respectively. For the sake of clarity, the H atoms not involved in the motifs shown have been omitted.

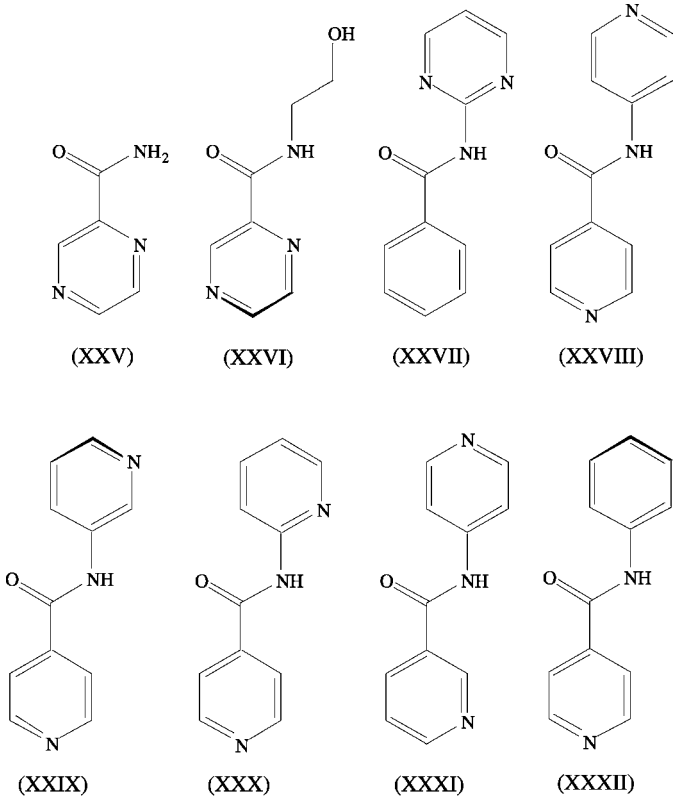
Compound (XXIV). The molecules of (XXIV), like those of (XVII), are linked by two C—H···O hydrogen bonds to form sheets, but the details of the sheet formation are entirely different in (XXIV) from those in (XVII). No centrosymmetric dimers can be identified in the structure of (XXIV), but instead the formation of the sheet can be analysed in terms of two one-dimensional substructures.

In the first substructure, the pyrazine C6 atom in the molecule at (x, y, z) acts as a hydrogen-bond donor to the nitro O151 atom in the molecule at ($1+x$, y, $1+z$), so generating by translation a $C(11)$ chain running parallel to the [101] direction. In the second substructure, the aryl C14 atom at (x, y, z) acts as a hydrogen-bond donor to the carbonyl O7 atom in the molecule at ($-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$), so forming a $C(8)$ chain running parallel to the [010] direction and generated by the 2_1 screw axis along (0, y, 0.25). The combination of the [101] and [010] chains generates a sheet lying parallel to ($10\bar{1}$) and taking the form of a (4,4) net built from a single type of $R_4^4(30)$ ring (Fig. 7*b*). There are no direction-specific interactions between adjacent sheets.

3.4. Related structures

The unsubstituted parent compound, pyrazinecarboxamide (XXV) (see below), has been reported to crystallize in at least four polymorphic forms, readily obtained under different crystallization conditions (Tamura *et al.*, 1961), and the structures of three of these polymorphs, designated as the α, β and δ forms, have been published (Takaki *et al.*, 1960; Rø & Sørum, 1972*a*,*b*). In each of these forms, pairs of molecules are linked into centrosymmetric $R_2^2(8)$ dimers built from paired N—H···O hydrogen bonds, and these dimers are then linked into chains of edge-fused rings, by N—H···N hydrogen bonds in the α polymorph (Takaki *et al.*, 1960) and by N—H···O hydrogen bonds in the β (Rø & Sørum, 1972*a*) and δ polymorphs (Rø & Sørum, 1972*b*). The molecular conformations in these polymorphs are all similar to those reported in this paper for *N*-arylpyrazinecarboxamides with an intramolecular N—H···N interaction. In the pyrazinecarboxamide polymorphs, the formation of this intramolecular interaction does not appear to preclude further participation in intermolecular hydrogen bonding by the N—H bond in question.

N-(2-Hydroxyethyl)pyrazinecarboxamide (XXVI) crystallizes with Z' = 2 in the space group $P\bar{1}$ (Zhang *et al.*, 2005): each of the independent molecules contains an intramolecular N—H···N hydrogen bond, although only one of these interaction is recorded in the table of hydrogen bonds. Despite the presence of these intramolecular interactions, the two independent N—H bonds both also participate in intermolecular N—H···N hydrogen bonding, although there are no N—H···O hydrogen bonds in the structure of this compound. A combination of two independent O—H···O hydrogen bonds and two independent intermolecular N—H···N hydrogen bonds link the molecules of (XXVI) into sheets.



Scheme 4

Compounds (XXVII) (Oertli *et al.*, 1992) and (XXVIII)–(XXXI) (Kumar *et al.*, 2004) are all isomeric with the parent compound of the series reported here, (I). In (XXVII), pairs of molecules are linked into centrosymmetric $R_2^2(8)$ dimers by paired N—H···N hydrogen bonds, while those in (XXVIII)–(XXXI) show considerable variation in supramolecular aggregation as the location of the ring N atoms is changed. In each of (XXVIII) and (XXX) the molecules are linked by N—H···N hydrogen bonds into $C(7)$ chains generated by glide planes: in (XXXI), which crystallizes with $Z' = 2$, the molecules are linked into $C_2^2(10)$ chains generated by translation and containing alternating N—H···O and N—H···N hydrogen bonds. The fourth of these isomers, (XXIX), crystallizes as a stoichiometric monohydrate, and the supramolecular aggregate takes the form of the three-dimensional framework structure containing N—H···O and O—H···N hydrogen bonds. None of the structures of (XXVII)–(XXXI) exhibits the $C(4)$ motif of N—H···O′═C hydrogen bonds so characteristic of simple amines. This motif is, however, present in (XXXII) (Kumar *et al.*, 2004); (XXXII) is, in fact, isostructural with the triclinic polymorph of benzanilide, and in these two compounds the molecules are linked into $C(4)$ chains generated by translation (Bowes *et al.*, 2003).

4. Concluding discussion

We comment briefly here on a few aspects of the structures reported in this paper, also making some comparisons with other cognate series, specifically involving the crystallization behaviour, the types and actions of the hydrogen bonds, and the effects of isomerism on the supramolecular structures.

Crystallization: The majority of the compounds studied here crystallize with $Z' = 1$; only (II) and the isostructural pair (III) and (XII) crystallize with $Z' = 2$, while the *Pc* polymorph of (X) is the sole example having $Z' > 2$; here $Z' = 4$. Only a single hydrate, (XV), has been observed within the present series. These observations may be contrasted with the findings of our recent two-dimensional study on *N*-isonicotinoyl arylaldehydehydrazones series (*K*) (see Scheme 1): in that series, around half of the examples crystallized with $Z' = 2$, and those carrying substituents at the 4-position of the aryl ring generally crystallized as hydrates, while for two compounds, both hydrated and anhydrous forms have been found, with both mono- and dihydrates found in a third example (Wardell *et al.*, 2007*b*).

Hydrogen bonding: The absence from the structures reported here of the $C(4)$ hydrogen-bond motif characteristic of simple carboxamides has already been noted (see §3.3). In fact, with the exception of the monohydrate, (XV), strong intermolecular hydrogen bonds of N—H···N and N—H···O types occur remarkably infrequently in the present series. Thus, intermolecular N—H···N hydrogen bonds occur only in the 2,6-difluorophenyl compound (XXI), where this hydrogen bond generates a $C(6)$ chain, and in the isostructural pair of compounds, the 3-methylphenyl derivative (III) and the 3-chlorophenyl derivative (XII), in each of which these interactions generate a $C_2^2(12)$ chain, reflecting the $Z' = 2$ value. In each of these three compounds, the N—H···N hydrogen bonds are augmented by C—H···N hydrogen bonds, so forming chains of rings (Figs. 5*a* and *b*).

In the remainder of the solvent-free structures, the supramolecular aggregation is dominated either by weak hydrogen bonds of C—H···N and C—H···O types, or by $\pi\cdots\pi$ stacking interactions. Weak hydrogen bonds in the absence of stacking interactions can generate rings, as in (V) and (XX), chains which are the dominant form of aggregation, or sheets as in (XVII) and (XXIV). Aromatic $\pi\cdots\pi$ stacking interactions can act alone to form chains, as in (II) and (XXIII), or they can link hydrogen-bonded chains into sheets, as in (IV) and (XIV). While there are no obvious similarities of behaviour between the aryl substituents of (V) and (XX), 2-trifluoromethyl in (V) *versus* 2,6-dimethyl in (XX), each of the sheet-forming compounds (XVII) and (XXIV) contains a nitro substituent and nitro O atoms act as hydrogen-bond acceptors in each case, leading to two-dimensional hydrogen-bonded structures. In the methoxy-substituted compounds (XIV) and (XV) the methoxy O atoms act as acceptors neither in strong hydrogen bonds nor in weak ones. The trifluoromethyl, fluoro and chloro substituents in (V), (VII), (X), (XII), (XIII) and (XXI)–(XXIII) play no role in the hydrogen bonding, nor would this be expected as covalent F and Cl bonded to organic C atoms are now known to be extremely weak hydrogen-bond acceptors (Howard *et al.*, 1996; Brammer *et al.*, 2001): hence apart from the nitro groups, the substituents in the aryl rings play no direct role in the formation of the hydrogen bonds.

It is striking that when chains are formed by a single C—H···O hydrogen bond, as in (I), (IV), (VII), (X*a*), (X*b*) and (XIII), the same donor atom C16 [or C*n*16 in (X*b*), for n = 1–4] and the same acceptor atom O7 [or O*n*7 in (X*b*) for n = 1–4] are involved in every such case. The chain is also always of the *C*(6) type generated by translation, along the [010] direction in (IV) and (X*a*), and along the [100] direction otherwise. Compound (I) contains an unsubstituted aryl ring while (IV), VII), (X) and (XIII) all contain a single substituent, respectively, CH_3, CF_3, F or Cl, at the 4-position of the aryl ring. These *C*(6) chains built from C—H···O hydrogen bonds are not found whenever there is a substituent, of whatever kind, occupying either a 2- or a 3-postion in the aryl ring: thus, for example, the structures of (XXII) and (XXIII) which carry substituents in the 2-positions as well as in the 4-positions contain no C—H···O hydrogen bonds and no *C*(6) chains.

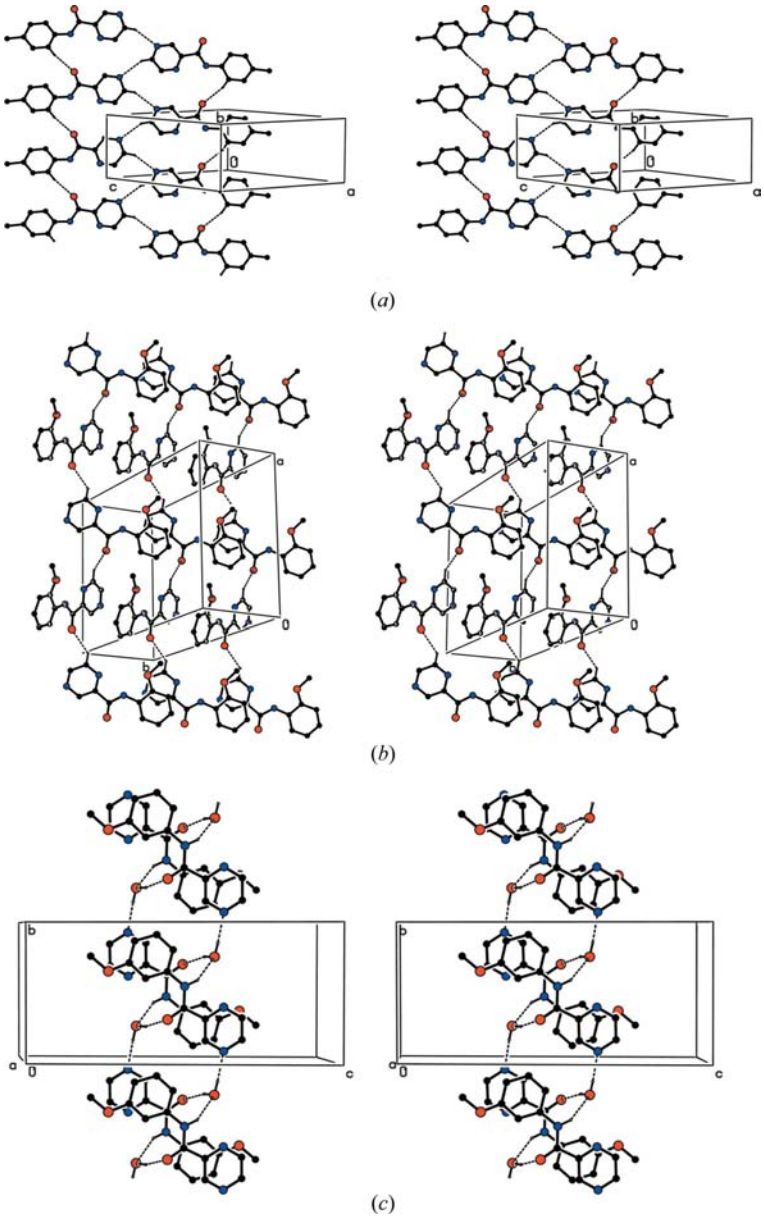


Figure 6
Stereoviews of parts of the crystal structures of compounds (IV), (XIV) and (XV): (*a*) one of the chains of edge-fused $R_3^3(18)$ rings in the 4-methylphenyl compound (IV), which forms sheets parallel to (100) by π-stacking; (*b*) a sheet parallel to (010) formed by π-stacking of hydrogen-bonded *C*(6) chains in the 2-methoxyphenyl compound (XIV); (*c*) one of the chains of edge-fused hydrogen-bonded $R_4^4(12)$ and $R_4^4(16)$ rings in the hydrated 3-methoxyphenyl compound (XV), which themselves form sheets parallel to (001) by π-stacking. For the sake of clarity, the H atoms not involved in the motifs shown have been omitted.

Isomerism. The isomeric methylphenyl compounds (II)–(IV) show rather little resemblance in the supramolecular behaviour beyond crystallization in the same space group. Thus, these isomers crystallize with Z' = 2 for isomers (II) and (III), but Z' = 1 for isomer (IV); while there are no intermolecular hydrogen bonds of any kind in the structure of isomer (II), that of isomer (II) contains both N—H···N and C—H···N hydrogen bonds, while the structure of isomer (IV) exhibits only C—H···O and C—H···N interactions; while aromatic $\pi\cdots\pi$ stacking interactions are present in the structures of both (II) and (IV), they are absent from that of isomer (III).

Although we have been unable to crystallize a full set of three positional isomers for any other of the substituents employed in this study, even the structures for the pairs of isomeric compounds which are available show differences as marked as those found for isomers (II)–(IV). Accordingly, in the isomeric trifluorophenyl compounds (V) and (VII), the 2-substituted isomer (V) forms cyclic dimers, whereas the 4-substituted isomer (VII) forms C(6) chains. In the chlorophenyl isomers (XII) and (XIII), strong N—H···N hydrogen bonds are present only for the 3-chlorophenyl isomer (XII) leading to the formation of a chain of rings, while the 4-chlorophenyl isomer (XIII) exhibits the *C*(6) chain formation apparently characteristic of the 4-substituted derivative in this series. The marked differences between the two methoxyphenyl isomers (XIV) and (XV) are dominated by the hydration of isomer (XV). Interchange of the two ring substituents in the isomers (XXII) and (XXIII) leads to marked differences in unit-cell shape, in space group, and in the intermolecular interactions; while intermolecular hydrogen bonds are absent from the structure of isomer (XXIII), there are *C*(9) chains generated by C—H···N hydrogen bonds in isomer (XXII).

Similarly, marked dependency on the position of the aryl substituent was noted in series (*K*) (Wardell *et al.*, 2007*b*). As a single, possibly extreme, example the 2-, 3- and 4-fluorophenyl derivatives in series (*K*) crystallize, respectively, in space groups $P\bar{1}$, *Pbca* and $P2_12_12_1$, with Z' values of 2, 2 and 1, and their hydrogen-bonded supramolecular structures are respectively one-dimen-

sional, three-dimensional and two-dimensional: no two of these isomers exhibit the same spectrum of direction-specific intermolecular interactions.

The differences both in the crystallization behaviour and in the supramolecular aggregation which are consequent upon very modest changes in molecular constitution, as observed both in the present series and in earlier related studies (Kelly *et al.*, 2002; Glidewell *et al.*, 2002; Glidewell *et al.*, 2004; Glidewell, Low, Skakle & Wardell, 2005; Wardell *et al.*, 2006; Glidewell, Low, Skakle, Wardell & Wardell, 2005; Cuffini *et al.*, 2006; de Souza *et al.*, 2005; Wardell *et al.*, 2007*b*) present keen tests for computational attempts to predict molecular crystal structures from first principles, an area where, despite much effort, convincing success remains elusive (Lommerse *et al.*, 2000; Motherwell *et al.*, 2002; Day *et al.*, 2005). The difficulty of structure prediction appears to be a characteristic of the crystal structures of molecular compounds where all of the intermolecular forces are comparatively weak, but of comparable magnitudes to the rotational energy barriers associated with single bonds, so that the molecular conformations are a direct reflection of the intermolecular interactions. For this reason alone, molecular conformations computed for isolated molecules are unlikely ever to reproduce the conformations observed experimentally in the crystalline state. Compounds whose molecules contain internal degrees of freedom such as rotations about single bonds, particularly where aryl and heteroaryl rings are connected to a semi-rigid unit, seem to pose particular difficulty in attempts at structure prediction, doubtless associated with the delicate interplay of intramolecular and intermolecular forces.

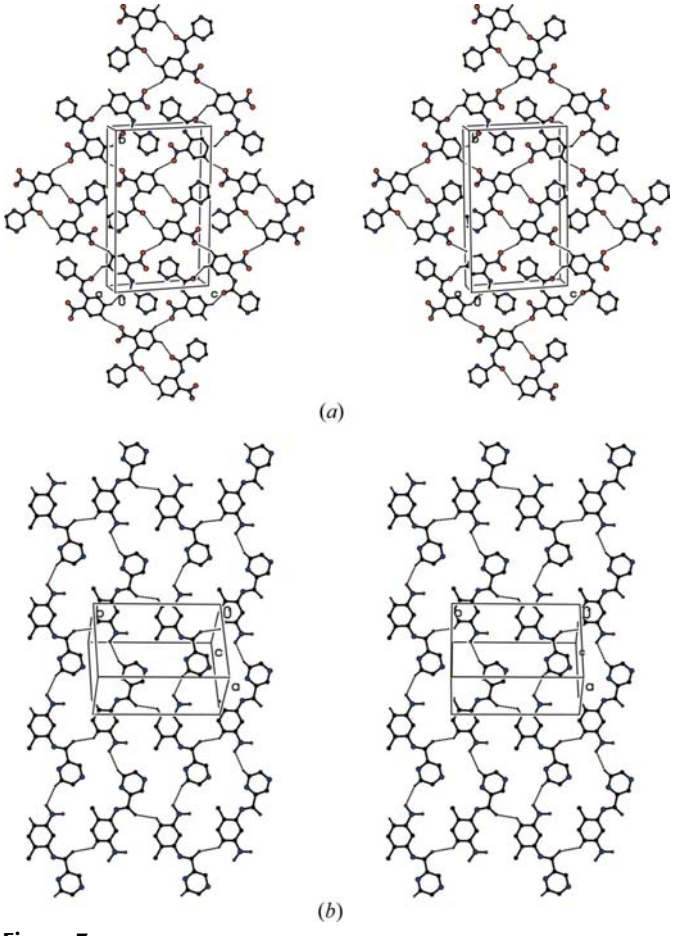


Figure 7
Stereoviews of the hydrogen-bonded sheets in (XVII) and (XXIV): (*a*) the sheet, parallel to (101), of $R_2^2(14)$ and $R_6^6(34)$ rings in the 2-nitrophenyl compound (XVII); (*b*) the sheet, parallel to (10$\bar{1}$), of $R_4^4(30)$ rings in the 2-methyl-5-nitrophenyl compound (XXIV). For the sake of clarity, the H atoms not involved in the motifs shown have been omitted.

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