organic compounds

Two different modes of halogen bonding in two 4-nitroimidazole derivatives

Maciej Kubicki[a]* and Paweł Wagner[b]

[a]Department of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland, and [b]Nanomaterials Research Centre, and MacDiarmid Institute for Advanced Materials and Nanotechnology, Massey University, Private Bag 11 222, Palmerston North, New Zealand
Correspondence e-mail: mkubicki@amu.edu.pl

In the crystal structures of the two imidazole derivatives 5-chloro-1,2-dimethyl-4-nitro-1H-imidazole, $C_5H_6ClN_3O_2$, (I), and 2-chloro-1-methyl-4-nitro-1H-imidazole, $C_4H_4ClN_3O_2$, (II), C—Cl···O halogen bonds are the principal specific interactions responsible for the crystal packing. Two different halogen-bond modes are observed: in (I), there is one very short and directional C—Cl···O contact [Cl···O = 2.899 (1) Å], while in (II), the C—Cl group approaches two different O atoms from two different molecules, and the contacts are longer [3.285 (2) and 3.498 (2) Å] and less directional. In (I), relatively short C—H···O hydrogen bonds provide the secondary interactions for building the crystal structure; in (II), the C—H···O contacts are longer but there is a relatively short π–π contact between molecules related by a centre of symmetry. The molecule of (I) is almost planar, the plane of the nitro group making a dihedral angle of 6.97 (7)° with the mean plane of the imidazole ring. The molecule of (II) has crystallographically imposed mirror symmetry and the nitro group lies in the mirror plane.

Comment

Halogen atoms covalently bound to a C atom can take part in the determination of crystal structure (*i.e.* the supramolecular architecture of molecular crystals) *via* interactions with the electron pairs of other atoms, interactions with other halogen atoms or acceptance of weak hydrogen bonds. The attractive interactions between halogens and atoms that have lone electron pairs have been known for some time (*e.g.* Hassel & Rømming, 1962; Bent, 1968; Dahl & Hassel, 1970; Hassel, 1970). This interaction was termed halogen bonding (Dumas *et al.*, 1983; Legon, 1998), in order to stress some geometrical correspondences with hydrogen bonding, for instance the striking tendency towards the linearity of the C—X···Y system [for reviews, see, for example, Legon (1999) and

Metrangolo *et al.* (2005)]. The halogen atom acts here as a Lewis acid. Database analysis (Lommerse *et al.*, 1996) and quantum mechanical calculations (Valerio *et al.*, 2000) allowed the 'acidity' of halogens to be characterized as I > Br > Cl, while fluorine generally does not participate in such interactions. Halogen bonds have been utilized successfully in the creation of supramolecular systems; for example, it has been shown that these interactions can create molecular tapes (Reddy, Panneerselvam *et al.*, 1993) or a diamondoid structure (Reddy, Craig *et al.*, 1993). They have also been used for designing molecular conductors (Imakubo *et al.*, 1998), host–guest systems (Messina *et al.*, 2001) and nonlinear optical crystals (George *et al.*, 2004). Intermolecular N···X interactions have also been found in solution (Wash *et al.*, 1999) and in the gas phase (Legon, 1999). Quite recently, experimental electron-density studies have clearly shown the presence of an interaction path and critical points connected with I···N and I···O interactions, and the results of these studies confirmed the electrostatic nature of halogen bonds (Bianchi *et al.*, 2003, 2004).

(1) X = Mc, Y = Cl
(II) X = Cl, Y = H
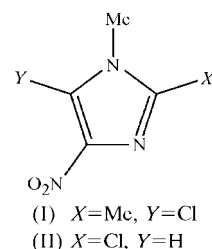
Allen *et al.* (1997) analyzed the halogen···O_{nitro} supramolecular synthon [in the sense defined by Desiraju (1995)] using both a crystallographic database and *ab initio* molecular orbital calculations. They found that in 46% of the crystal structures containing both C—NO₂ and C—X (X = Cl, Br or I) fragments there are X···O contacts shorter than the sum of the van der Waals radii plus 0.2 Å. Following Desiraju *et al.*
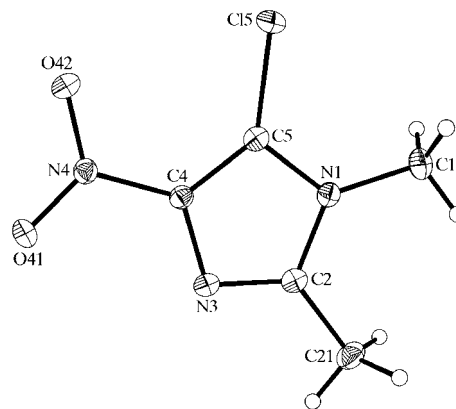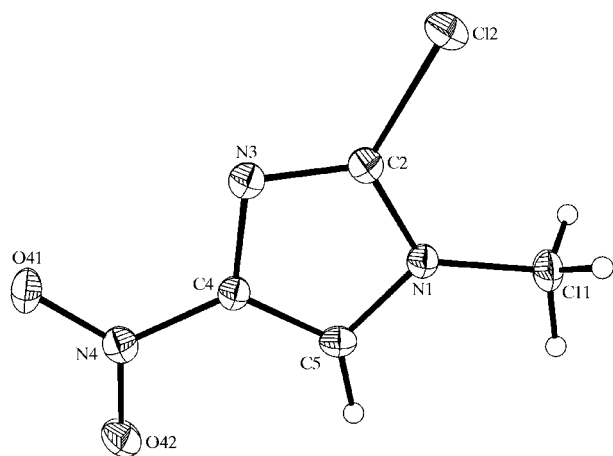

Figure 1
An anisotropic displacement ellipsoid representation of the molecule of (I), together with the atom-labelling scheme (Siemens, 1989). The ellipsoids are drawn at the 50% probability level and H atoms are depicted as spheres with arbitrary radii.

(1993), three types of halogen-bond system were defined. In the first two cases, the approach of a halogen atom to a nitro group is such that both $X\cdots O$ lines are *trans* to the C—N bond, forming (i) a symmetrical bifurcated motif, with $X\cdots O1 \simeq X\cdots O2$, or (ii) an asymmetric motif, where one of the distances is so long that there is no interaction. Possibility (iii) is a *cis* approach to one of the O atoms. The results of this analysis show also that for chlorine there is a strong tendency to form 'monocoordinate interactions' (ii) or (iii), with only one O atom, rather than bifurcated contacts with both O atoms as in (i). This latter arrangement is typical for iodine and to some extent for bromine; such an almost symmetrical bifurcated halogen bond was found in a similar imidazole derivative, *viz.* 1-(4-bromophenyl)-2-methyl-4-nitroimidazole (Kubicki, 2004).

In the course of our studies of weak intermolecular interactions in the crystal structures of simple 4-nitroimidazole derivatives (nitroimidazoles and especially chloronitroimidazoles can be used as radiosensitizers of hypoxic cells; *e.g.* Widel *et al.*, 1987), we have determined the crystal structures of two closely related compounds, *viz.* 5-chloro-1,2-dimethyl-4-nitro-1H-imidazole, (I), and 2-chloro-1-methyl-4-nitro-1H-imidazole, (II). In both these compounds, halogen bonds of the C—Cl$\cdots$O$_{nitro}$ type are the driving force of the supramolecular architecture.

In (I), the imidazole ring is planar, with a maximum deviation of 0.037 (6) Å, and the closest substituent atoms (*i.e.* except for the O atoms) are almost coplanar with the ring [the maximum deviation from the plane, for atom C11, is 0.059 (2) Å]. The nitro group is twisted by 6.97 (7)° with respect to the imidazole ring (Fig. 1). The molecule of (II) occupies a special position; it lies on a mirror plane and therefore is perfectly planar (Fig. 2). There are no traces of disorder or strangely shaped displacement ellipsoids, which might suggest the statistical nature of this mirror plane. The

same is true at room temperature, so it seems that in this temperature range there is no phase transition (of order–disorder nature). The molecular dimensions are close to typical, with a notable influence of the type of substituents on the intramolecular N1—C2—N3 angles (Table 1). The typical asymmetry of the C—N—O angles can also be observed here (*cf.* Kubicki, 2005).

In both structures, C—Cl$\cdots$O halogen bonds are the most important factor in the crystal packing. Noticeably, in neither of the structures does the imidazole N atom take part in the halogen bonding. This is in agreement with our observation (in high-resolution studies of the crystal structure of 1-phenyl-4-nitroimidazole) that the electron density of the lone pairs is higher at the O atoms than at the imidazole N atom (Kubicki *et al.*, 2002).

The types of interaction are different in both cases. For a description of the networks created by intermolecular interactions, it will be useful to apply the graph-set notation (Etter *et al.*, 1990; Bernstein *et al.*, 1995). We will follow Bryant *et al.* (1998) and regard the Cl$\cdots$O interactions as pseudo-hydrogen bonds, with Cl as a donor and O as an acceptor. In (I), there is one very short and linear interaction of the *cis* type (Fig. 3 and Table 2). It is actually one of the shortest interactions of this type found in the Cambridge Structural Database (CSD; Allen, 2002). This interaction should be classified as belonging to type (iii) of those listed earlier. These halogen bonds connect the molecules into infinite chains along the [010] direction. The motif created by these interactions can be described as $C_1^1(5)$.
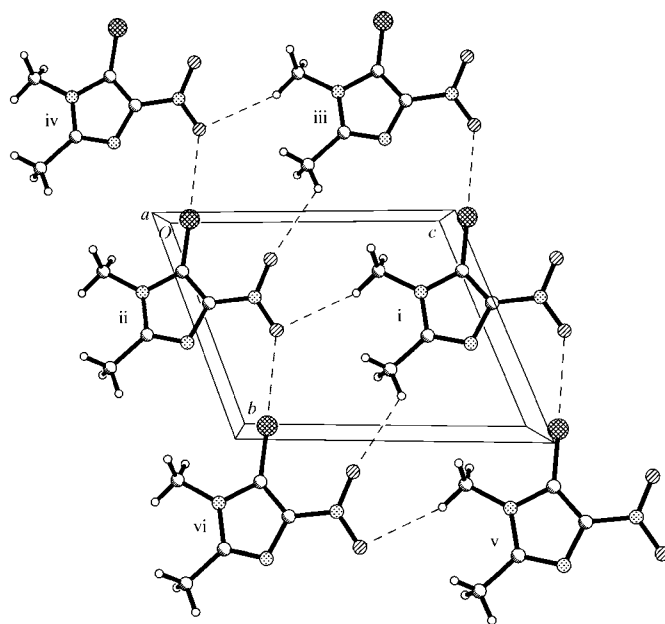

Figure 2
An anisotropic displacement ellipsoid representation of the molecule of (II), together with the atom-labelling scheme (Siemens, 1989). The ellipsoids are drawn at the 50% probability level and H atoms are depicted as spheres with arbitrary radii.
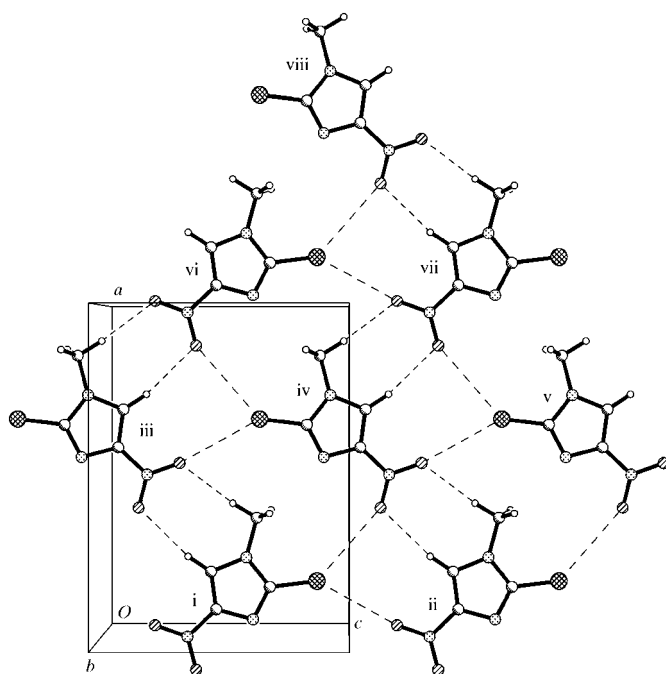

Figure 3
The layer created by halogen and weak hydrogen bonds in (I) (Siemens, 1989), as seen along the *a* direction. Intermolecular interactions are depicted as dashed lines. [Symmetry codes: (i) x, y, z; (ii) $x, y, z - 1$; (iii) $x, y - 1, z$; (iv) $x, y - 1, z - 1$; (v) $x, y + 1, z$; (vi) $x, y + 1, z - 1$.]

organic compounds

In (II), the interaction is of another kind. The C—Cl bond approaches two O atoms at moderate distances (Fig. 4 and Table 2), and both approaches are of *cis* type, because these two O atoms are from two different molecules. Therefore, it belongs – in principle – to type (iii), but the bifurcated nature of this contact allows the creation of a subtype, (iii*a*). In the CSD, we have found 69 hits with this motif. These halogen bonds connect molecules into two-dimensional layers in the *ab* plane (on a mirror plane of symmetry; Fig. 4). This structure is much more complicated than that in (I). There are first-rank (*i.e.* built of only one type of interactions) chains, *viz.* $C_1^1(6)$ parallel to *a* and $C_1^1(6)$ parallel to *c*. These chains interweave and produce second-rank (built of two different interactions) motifs, *e.g.* $C_2^2(8)$ chains along *a* and closed structures of the $R_3^4(16)$ type.

The halogen-bonded arrays are further expanded by means of weak C—H···O interactions (Table 2). In (I), these bonds connect neighbouring chains into layers, closing consecutive $R_2^3(12)$ rings (Fig. 3). In this structure, additional π–π interactions between the imidazole rings connected by a centre of symmetry create the bilayers. The distance between the centres of the rings (which are parallel by symmetry) is 3.314 (2) Å, and taking the offset into account the distance between the planes is 3.27 Å. In (II), the weak hydrogen bonds additionally strengthen the halogen-bonded layers, creating $R_2^2(8)$ ring motifs. The mirror planes occupied by these layers are *b*/2 apart (3.07 Å), but the layers are shifted in such a way that the ring planes do not overlap at all.

Figure 4
The layer created by halogen and weak hydrogen bonds in (II) (Siemens, 1989), as seen along the *b* direction. Intermolecular interactions are depicted as dashed lines. [Symmetry codes: (i) x, y, z; (ii) $x, y, z + 1$; (iii) $x + \frac{1}{2}, y, -z + \frac{1}{2}$; (iv) $x + \frac{1}{2}, y, -z + \frac{3}{2}$; (v) $x + \frac{1}{2}, y, -z + \frac{5}{2}$; (vi) $x + 1, y, z$; (vii) $x + 1, y, z + 1$; (viii) $x + \frac{3}{2}, y, -z + \frac{3}{2}$.]

Compound (I)

Crystal data

$C_5H_6ClN_3O_2$	$\gamma = 71.305 (14)°$
$M_r = 175.58$	$V = 355.19 (10)$ Å^3
Triclinic, $P\bar{1}$	$Z = 2$
$a = 6.8119 (10)$ Å	Mo $K\alpha$ radiation
$b = 7.0301 (12)$ Å	$\mu = 0.49$ mm^{-1}
$c = 8.5403 (13)$ Å	$T = 100 (1)$ K
$\alpha = 66.631 (16)°$	$0.15 \times 0.1 \times 0.1$ mm
$\beta = 80.204 (13)°$	

Data collection

Kuma KM-4 CCD four-circle diffractometer	3402 measured reflections
Absorption correction: multi-scan (*SORTAV*; Blessing, 1989)	1767 independent reflections
	1565 reflections with $I > 2\sigma(I)$
$T_{min} = 0.895$, $T_{max} = 0.944$	$R_{int} = 0.040$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.025$	124 parameters
$wR(F^2) = 0.066$	All H-atom parameters refined
$S = 1.08$	$\Delta\rho_{max} = 0.34$ e Å^{-3}
1767 reflections	$\Delta\rho_{min} = -0.38$ e Å^{-3}

Compound (II)

Crystal data

$C_4H_4ClN_3O_2$	$V = 622.26 (8)$ Å^3
$M_r = 161.55$	$Z = 4$
Orthorhombic, *Pnma*	Mo $K\alpha$ radiation
$a = 11.6550 (9)$ Å	$\mu = 0.55$ mm^{-1}
$b = 6.1372 (5)$ Å	$T = 100 (1)$ K
$c = 8.6994 (6)$ Å	$0.2 \times 0.15 \times 0.1$ mm

Data collection

Kuma KM-4 CCD four-circle diffractometer	6383 measured reflections
Absorption correction: multi-scan (*SORTAV*; Blessing, 1989)	922 independent reflections
	696 reflections with $I > 2\sigma(I)$
$T_{min} = 0.940$, $T_{max} = 0.944$	$R_{int} = 0.034$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.030$	71 parameters
$wR(F^2) = 0.065$	All H-atom parameters refined
$S = 1.01$	$\Delta\rho_{max} = 0.26$ e Å^{-3}
922 reflections	$\Delta\rho_{min} = -0.31$ e Å^{-3}

Table 1
Selected geometrical parameters (Å, °).

	(I)	(II)
C2—N1—C5	106.8 (1)	106.4 (2)
C2—N3—C4	104.6 (1)	102.7 (2)
N3—C2—N1	111.91 (9)	113.75 (18)
C4—N4—O41	118.9 (1)	119.0 (2)
C4—N4—O42	117.9 (1)	117.0 (2)
N3—C4—N4	122.0 (1)	121.5 (2)
C5—C4—N4	126.9 (2)	125.6 (2)
N3—C4—N4—O41	6.9 (1)	0
N3—C4—N4—O42	−173.3 (1)	180
Imidazole/NO2	6.97 (7)	0

Table 2
Halogen- and hydrogen-bond data (Å, °).

C—Cl···O	C—Cl	Cl···O	C—Cl···O	C—N—O···Cl
(I)				
C5—Cl5···O41^i	1.690 (1)	2.899 (1)	175.90 (4)	−5.4 (1)
(II)				
C2—Cl2···O42^{ii}	1.701 (2)	3.285 (2)	144.3 (1)	0
C2—Cl2···O41^{iii}	1.701 (2)	3.498 (2)	138.0 (1)	0

D—H···A	D—H	H···A	D···A	D—H···A
(I)				
C11—H11C···O41^{iv}	0.94 (2)	2.66 (2)	3.545 (2)	157 (2)
C21—H21A···O42^v	0.94 (2)	2.67 (2)	3.318 (2)	126 (1)
(II)				
C11—H11A···O42^{vi}	1.01 (2)	2.40 (2)	3.405 (1)	175 (2)
C5—H5···O41^{vii}	0.99 (3)	2.50 (3)	3.475 (2)	169 (3)

Symmetry codes: (i) $x, y − 1, z$; (ii) $x, y, z + 1$; (iii) $x + \frac{1}{2}, y, −z + \frac{3}{2}$; (iv) $x, y, z − 1$; (v) $x, y + 1, z + 1$; (vi) $x + \frac{1}{2}, y, −z + \frac{3}{2}$; (vii) $x + \frac{1}{2}, y, −z + \frac{1}{2}$; (ix) $−x + 1, y + \frac{1}{2}, −z + \frac{3}{2}$; (x) $x, −y + \frac{3}{2}, z + \frac{1}{2}$; (xi) $x, y − 1, z$.

H atoms were freely refined [C—H = 0.93 (2)–1.005 (18) Å in (I) and 0.90 (2)–1.01 (3) Å in (II)].

For both compounds, data collection: *CrysAlis CCD* (Oxford Diffraction, 2002); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989); software used to prepare material for publication: *SHELXL97*.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Allen, F. H., Lommerse, J. P. M., Hoy, V. J., Howard, J. A. K. & Desiraju, G. R. (1997). *Acta Cryst.* B**53**, 1006–1016.
Bent, H. A. (1968). *Chem. Rev.* **68**, 587–648.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bianchi, R., Forni, A. & Pilati, T. (2003). *Chem. Eur. J.* **9**, 1631–1638.
Bianchi, R., Forni, A. & Pilati, T. (2004). *Acta Cryst.* B**60**, 559–568.
Blessing, R. H. (1989). *J. Appl. Cryst.* **22**, 396–397.
Bryant, R., James, S. C., Norman, N. C. & Orpen, A. G. (1998). *Acta Cryst.* C**54**, 1113–1115.
Dahl, T. & Hassel, O. (1970). *Acta Chem. Scand.* **24**, 377–382.
Desiraju, G. R. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 2311–2327.
Desiraju, G. R., Pedireddi, V. R., Sarma, J. A. R. P. & Zacharias, D. E. (1993). *Acta Chim. Hung.* **130**, 451–465.
Dumas, J. M., Gomel, L. & Guerin, M. (1983). *The Chemistry of Functional Groups*, Suppl. D, edited by S. Patai & Z. Rappaport, pp. 985–1020. New York: Wiley.
Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* B**46**, 256–262.
George, S., Nangia, A., Lam, C.-K., Mak, T. C. W. & Nicoud, J.-F. (2004). *Chem. Commun.* pp. 1202–1203.
Hassel, O. (1970). *Science*, **170**, 497–502.
Hassel, O. & Rømming, C. (1962). *Q. Rev. Chem. Soc.* **16**, 1–13.
Imakubo, T., Maruyama, T., Sawa, H. & Kobayashi, K. (1998). *Chem. Commun.* pp. 2021–2022.
Kubicki, M. (2004). *Acta Cryst.* **60**, o341–o343.
Kubicki, M. (2005). *J. Mol. Struct.* **743**, 209–215.
Kubicki, M., Borowiak, T., Dutkiewicz, G., Souhassou, M., Jelsch, C. & Lecomte, C. (2002). *J. Phys. Chem. B*, **106**, 3706–3714.
Legon, A. C. (1998). *Chem. Eur. J.* **4**, 1890–1897.
Legon, A. C. (1999). *Angew. Chem. Int. Ed.* **38**, 2687–2714.
Lommerse, J. P. M., Stone, A. J., Taylor, R. & Allen, F. H. (1996). *J. Am. Chem. Soc.* **118**, 3108–3116.
Messina, M. T., Metrangolo, P., Panzeri, W., Pilati, T. & Resnati, G. (2001). *Tetrahedron*, **57**, 8543–8550.
Metrangolo, P., Neukirch, H., Pilati, T. & Resnati, G. (2005). *Acc. Chem. Res.* **38**, 386–395.
Oxford Diffraction (2002). *CrysAlis CCD* and *CrysAlis RED*. Versions 1.169. Oxford Diffraction, Wrocław, Poland.
Reddy, D. S., Craig, D. C., Rae, A. D. & Desiraju, G. R. (1993). *J. Chem. Soc. Chem. Commun.* pp. 1737–1739.
Reddy, D. S., Panneerselvam, K., Pilati, T. & Desiraju, G. R. (1993). *J. Chem. Soc. Chem. Commun.* pp. 661–662.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Siemens (1989). *Stereochemical Workstation Operation Manual.* Release 3.4. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Suwiński, J., Salwińska, E., Watras, J. & Widel, M. (1982). *Pol. J. Chem.* **56**, 1261–1272.
Valerio, G., Raos, G., Meille, S. V., Metrangolo, P. & Resnati, G. (2000). *J. Phys. Chem. A*, **104**, 1617–1620.
Wash, P. L., Ma, S., Obst, U. & Rebek, J. Jr (1999). *J. Am. Chem. Soc.* **121**, 7973–7974.
Widel, M., Watras, J., Suwiński, J. & Salwińska, E. (1987). *Neoplasma*, **34**, 241–251.