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# Supramolecular structures of 2-cyano-3-dimethylamino-*N*-(4-methylphenyl)acrylamide and 2-cyano-3-dimethylamino-*N*-(2-methoxyphenyl)acrylamide

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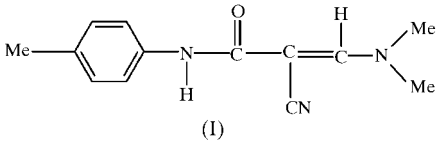
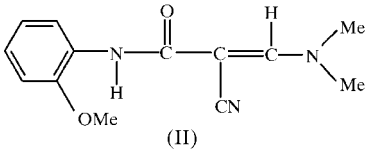
In the title compounds, $C_{13}H_{15}N_3O$, (I), and $C_{13}H_{15}N_3O_2$, (II), the dihedral angles between the planes of the phenyl ring and the amide group are 4.1 (1) and 20.7 (1)°, respectively. The molecules adopt a fully extended conformation, aided by intramolecular interactions. The molecular structures of (I) and (II) display different crystal packing and hydrogen-bonding networks.

## Comment

As part of our study of conformational analysis, crystallographic work on *N*-aromatic amide derivatives has been undertaken. These derivatives are analogs of the active metabolites of the immunosuppressive drug leflunomide, which are known to act, in part, by inhibiting the tyrosine




(I)




(II)

kinase epidermal growth-factor receptor (EGFR; Mattar *et al.*, 1993). EGFR is a membrane-associated tyrosine kinase, which serves as an endogenous negative regulator of apoptosis in breast cancer cells (Uckun *et al.*, 1998). The present study reports the structures of two *N*-acrylamide compounds, (I) and (II) (Figs. 1 and 2), in order to examine the effects of substituents on the hydrogen-bonding systems and on the crystal structures.

The dihedral angle between the planes of the phenyl rings and the amide groups are 4.1 (1) and 20.7 (1)° for (I) and (II), respectively. In both compounds, the geometry of the amide group is comparable to that of similar groups in acetanilides (Haisa *et al.*, 1977). The C10—C11 and C11—N12 bond lengths (Tables 1 and 3) agree with expected C$sp^2$—C$sp$ [1.431 (14) Å] and C$sp$—N [1.136 (10) Å] bond lengths, respectively (Allen *et al.*, 1987). Similar observations have been noted for the crystal structures of the leflunomide metabolite analogs (Ghosh *et al.*, 1999; Ghosh & Uckun, 1999) and for an acrylamide derivative (Ompraba *et al.*, 2003). In (II), the C2—O17—C18 angle [118.3 (1)°] is close to that expected for $sp^2$ hybridization of atom O17. The distortion and enlargement of the C6—C1—N7, C1—N7—C8 and N7—C8—O9 angles from the trigonal value (120°) are due to intramolecular C6—H6···O9 hydrogen bonds (Tables 2 and 4). In both (I) and (II), the cyanoacrylamide side chain is planar, with $\pi$-conjugation along the chain causing variations of the bond distances with respect to localized double and single bonds. The C1—N7—C8—C10 torsion angle does not differ significantly between (I) and (II) [−178.9 (1) and 176.6 (1)°, respectively], whereas the C6—C1—N7—C8 angle differs substantially [−3.7 (3) and −20.2 (2)°, respectively], indicating that the large twist around the C1—N7 bond in (II) is due to an intramolecular N7—H7···O17 hydrogen bond. This hydrogen bond determines the orientation of the

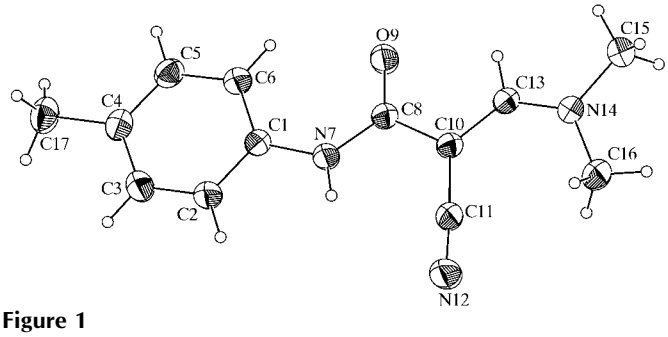



**Figure 1**
The molecular structure of (I), showing displacement ellipsoids at the 35% probability level.

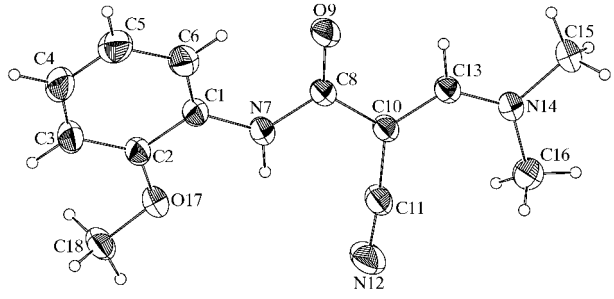



**Figure 2**
The molecular structure of (II), showing displacement ellipsoids at the 35% probability level.

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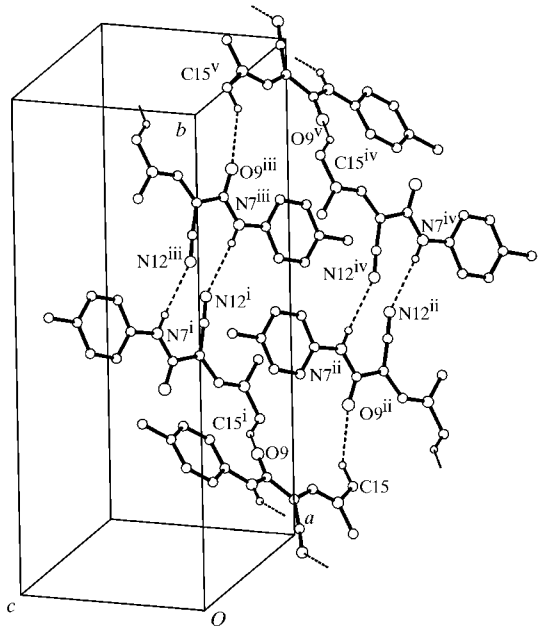


**Figure 3**
A view of the discrete hexamer formed by the molecules of (I). [Symmetry codes: (i) $x, \frac{1}{2}-y, \frac{1}{2}+z$; (ii) $x, \frac{1}{2}-y, -\frac{1}{2}+z$; (iii) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $2-x, \frac{1}{2}+y, -\frac{1}{2}-z$; (v) $2-x, 1-y, -z$.]

methoxy group [C1—C2—O17—C18 = 179.5 (1)°], which is coplanar with the phenyl ring.

The supramolecular structures of (I) and (II) are completely different. In (I), the symmetry-related molecules are linked together head-to-tail *via* N7—H7···N12($2-x$, $-y$, $z$) hydrogen bonds to form a dimer comprising an $R_2^2(12)$ ring (Bernstein *et al.*, 1995). The dimers at ($x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$) and ($2-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$) [center of symmetry at (1, $\frac{1}{2}$, $\frac{1}{2}$)], and ($x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) and ($2-x$, $\frac{1}{2}+y$, $-\frac{1}{2}-z$) [center of symmetry at (1, $\frac{1}{2}$, $-\frac{1}{2}$)], are further linked by symmetry-related C—H···O hydrogen bonds, linking atom O9 at ($x$, $y$, $z$) with atom H15*A* at ($x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$), atom H15*A* at ($x$, $y$, $z$) with atom O9 at ($x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$), atom O9 at ($2-x$, $1-y$, $-z$) with atom H15*A* at ($2-x$, $\frac{1}{2}+y$, $-\frac{1}{2}-z$), and atom H15*A* at ($2-x$, $1-y$, $-z$) with atom O9 at ($2-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$), respectively, thus forming an $R_6^6(36)$ ring. Hence, a discrete hexamer is formed with the center of symmetry at (1, $\frac{1}{2}$, 0) (Fig. 3). The result is a two-dimensional layer, which runs along the *bc* plane (Fig. 4). In (II), an intramolecular N7—H7···O17 hydrogen bond forms a five-membered ring. A $C(8)$ motif is formed *via* a C4—H4···O9($1-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$) hydrogen bond, creating a chain that runs parallel to the *ab* plane. Two such antiparallel chains are shown in Fig. 5. A C—H···$\pi$ interaction is also observed in (II) (Table 4). The H7···C11 distances, *viz.* 2.34 Å in (I) and 2.28 Å in (II), are short as a result of the positive charge on atom H7 and the negative charge on atom C11.

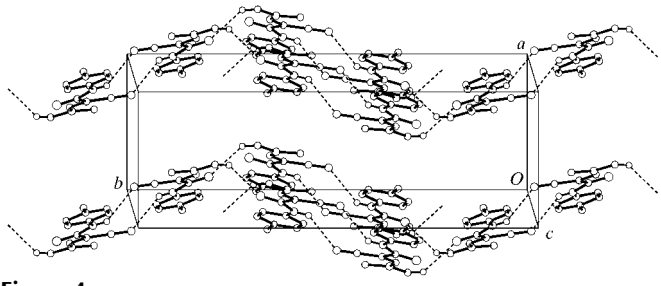


**Figure 4**
The molecular packing of (I), viewed along the *c* axis.

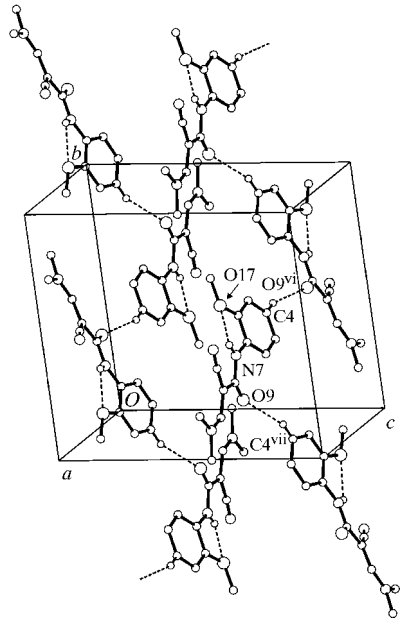


**Figure 5**
A view of the crystal structure of (II), viewed along the *a* axis, showing two antiparallel $C(8)$ chains. [Symmetry codes: (vi) $1-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$; (vii) $1-x$, $-\frac{1}{2}+y$, $\frac{3}{2}-z$.]

## Experimental

Substituted *N*-arylcyanoacetamide (0.005 mol) was dissolved in dimethylformamide (6 ml) and kept under ice-cold conditions. To this solution, $POCl_3$ (1.4 ml, 0.015 mol) was added slowly with stirring. The reaction mixture was allowed to reach room temperature and was stirred for 3–4 h. The residue was then poured on to crushed ice and neutralized with NaOH (10%), and the crude product was filtered, washed with water and dried. Finally, the compound was purified by recrystallization using an ethyl acetate–petroleum ether mixture [m.p. 445 and 425 K for (I) and (II), respectively].

### Compound (I)

*Crystal data*

$C_{13}H_{15}N_3O$
$M_r = 229.28$
Monoclinic, $P2_1/c$
$a = 7.5846$ (3) Å
$b = 22.4477$ (10) Å
$c = 7.5989$ (3) Å
$\beta = 106.306$ (1)°
$V = 1241.72$ (9) Å$^3$
$Z = 4$
$D_x = 1.226$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 4951 reflections
$\theta = 1.8$–28.3°
$\mu = 0.08$ mm$^{-1}$
$T = 293$ (2) K
Slab, pale yellow
0.48 × 0.40 × 0.16 mm

*Data collection*

Siemens SMART CCD area-detector diffractometer
$\omega$ scans
8417 measured reflections
3022 independent reflections
2242 reflections with $I > 2\sigma(I)$
$R_{int} = 0.037$
$\theta_{max} = 28.3°$
$h = -10 \rightarrow 8$
$k = -29 \rightarrow 27$
$l = -10 \rightarrow 8$

**Table 1**
Selected geometric parameters (Å, °) for (I).

| | | | |
|---|---|---|---|
| C1—N7 | 1.415 (2) | C11—N12 | 1.148 (2) |
| N7—C8 | 1.364 (2) | C13—N14 | 1.320 (2) |
| C8—O9 | 1.228 (2) | | |
| | | | |
| C6—C1—N7 | 124.6 (2) | N14—C13—C10 | 132.0 (2) |
| C2—C1—N7 | 117.0 (1) | C13—N14—C16 | 124.1 (2) |
| C8—N7—C1 | 128.4 (1) | C13—N14—C15 | 120.4 (2) |
| O9—C8—N7 | 122.5 (2) | C16—N14—C15 | 115.5 (2) |
| | | | |
| C6—C1—N7—C8 | −3.7 (3) | N7—C8—C10—C13 | −170.2 (1) |
| C1—N7—C8—C10 | −178.9 (1) | C11—C10—C13—N14 | 0.1 (3) |

**Table 2**
Hydrogen-bonding geometry (Å, °) for (I).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| C6—H6···O9 | 0.93 | 2.27 | 2.864 (2) | 121 |
| C13—H13···O9 | 0.93 | 2.34 | 2.748 (2) | 106 |
| N7—H7···N12$^{viii}$ | 0.86 | 2.50 | 3.228 (2) | 143 |
| C15—H15*A*···O9$^{ii}$ | 0.96 | 2.57 | 3.360 (2) | 139 |

Symmetry codes: (ii) $x, \frac{1}{2}-y, -\frac{1}{2}+z$; (viii) $2-x, -y, -z$.

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0849P)^2 + 0.2309P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R[F^2 > 2\sigma(F^2)] = 0.057$ | $(\Delta/\sigma)_{max} < 0.001$ |
| $wR(F^2) = 0.169$ | $\Delta\rho_{max} = 0.19$ e Å$^{-3}$ |
| $S = 1.04$ | $\Delta\rho_{min} = -0.15$ e Å$^{-3}$ |
| 3022 reflections | |
| 157 parameters | |
| H-atom parameters constrained | |

## Compound (II)

*Crystal data*

| | |
|---|---|
| $C_{13}H_{15}N_3O_2$ | $D_x = 1.221$ Mg m$^{-3}$ |
| $M_r = 245.28$ | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1/c$ | Cell parameters from 5915 reflections |
| $a = 7.5141$ (3) Å | $\theta = 2.2$–$28.3°$ |
| $b = 12.7580$ (6) Å | $\mu = 0.09$ mm$^{-1}$ |
| $c = 13.9381$ (6) Å | $T = 293$ (2) K |
| $\beta = 92.795$ (1)° | Block, pale yellow |
| $V = 1334.58$ (10) Å$^3$ | 0.48 × 0.46 × 0.42 mm |
| $Z = 4$ | |

*Data collection*

| | |
|---|---|
| Siemens SMART CCD area-detector diffractometer | $R_{int} = 0.041$ |
| $\omega$ scans | $\theta_{max} = 28.3°$ |
| 9025 measured reflections | $h = -9 \rightarrow 9$ |
| 3278 independent reflections | $k = -16 \rightarrow 16$ |
| 2425 reflections with $I > 2\sigma(I)$ | $l = -12 \rightarrow 18$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0825P)^2 + 0.0796P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R[F^2 > 2\sigma(F^2)] = 0.048$ | $(\Delta/\sigma)_{max} < 0.001$ |
| $wR(F^2) = 0.152$ | $\Delta\rho_{max} = 0.19$ e Å$^{-3}$ |
| $S = 1.05$ | $\Delta\rho_{min} = -0.14$ e Å$^{-3}$ |
| 3278 reflections | |
| 166 parameters | |
| H-atom parameters constrained | |

**Table 3**
Selected geometric parameters (Å, °) for (II).

| | | | |
|---|---|---|---|
| C1—N7 | 1.407 (2) | C11—N12 | 1.147 (2) |
| N7—C8 | 1.368 (2) | C13—N14 | 1.316 (2) |
| C8—O9 | 1.228 (2) | | |
| | | | |
| C6—C1—N7 | 124.6 (1) | N14—C13—C10 | 130.8 (1) |
| N7—C1—C2 | 115.7 (1) | C13—N14—C16 | 123.8 (1) |
| C8—N7—C1 | 128.4 (1) | C13—N14—C15 | 120.1 (1) |
| O9—C8—N7 | 122.2 (1) | C16—N14—C15 | 116.1 (1) |
| | | | |
| C6—C1—N7—C8 | −20.2 (2) | C11—C10—C13—N14 | 3.4 (2) |
| C1—N7—C8—C10 | 176.6 (1) | C1—C2—O17—C18 | 179.5 (1) |
| N7—C8—C10—C13 | 177.3 (1) | | |

**Table 4**
Hydrogen-bonding geometry (Å, °) for (II).

*Cg* is the centroid of the C1–C6 ring.

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| C6—H6···O9 | 0.93 | 2.38 | 2.910 (2) | 116 |
| C13—H13···O9 | 0.93 | 2.36 | 2.756 (2) | 106 |
| N7—H7···O17 | 0.86 | 2.22 | 2.596 (1) | 106 |
| C4—H4···O9$^{vi}$ | 0.93 | 2.57 | 3.452 (2) | 158 |
| C18—H18*C*···*Cg*$^{ix}$ | 0.96 | 2.75 | 3.551 (1) | 141 |

Symmetry codes: (vi) $1-x, \frac{1}{2}+y, \frac{3}{2}-z$; (ix) $1-x, 1-y, 1-z$.

For both compounds, data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; structure solution: *SHELXS*97 (Sheldrick, 1997); structure refinement: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1594). Services for accessing these data are described at the back of the journal.

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