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Structural motifs in acetoacetanilides: the effect of a fluorine substituent

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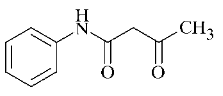
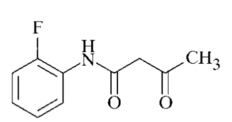
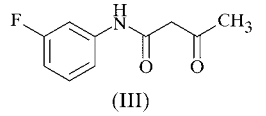
The structures of three fluoro-substituted acetoacetanilides, namely 2′-, 3′- and 4′-fluoroacetoacetanilide, all $C_{10}H_{10}FNO_2$, are presented and discussed. We observe a planar structure with intramolecular hydrogen bonding when the F atom is in the *ortho* position of the aromatic ring, and a twisted structure with intermolecular hydrogen bonding when the F atom is in the *meta* or *para* positions. It can be predicted which of these two structural motifs will be adopted by considering the position of any aromatic substituents. In this regard, fluorine appears to mimic the steric effect of a larger substituent, which we attribute to its high electronegativity.

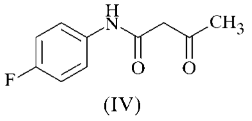
Comment

Acetoacetanilides are common starting materials in the synthesis of azo pigments. Typically during the synthesis of such a pigment, a diazonium salt component is added to a slightly acidic aqueous slurry of the anilide. Thus, the solid-state properties of the anilide may play a role in determining the final quality of the pigment. Acetoacetanilide, (I), and compounds derived from it by substitution around the aryl ring, thus give rise to a wide range of commercial azo pigments. Such azo pigments are of varying yellow and orange shades and moderate fastness properties, and find applications in a range of systems, including the colouration of inks, paints and plastics (Herbst & Hunger, 1993).


(I)


(II)


(III)


(IV)

We recently compared the structures of some commercially important acetoacetanilides with those of the monoazo pigments derived from them (Chisholm *et al.*, 2000). To expand further our knowledge of the packing motifs for such compounds, we have prepared the fluorinated compounds 2′-fluoroacetoacetanilide, (II), 3′-fluoroacetoacetanilide, (III), and 4′-fluoroacetoacetanilide, (IV), and determined the single-crystal structure for each of them.

The presence of fluorine in molecular crystals and its influence on crystal packing have been comparatively rarely studied [for examples, see Hayashi & Mori (1998) and Renak *et al.* (1999)], given the wealth of information available on the effect of the F atom in biological chemistry (Filler *et al.*, 1993). The interactions of organic fluorine with other atoms within a crystal lattice are weak and, indeed, it has been observed that, when organically bonded, fluorine hardly ever acts as a hydrogen-bond acceptor (Dunitz & Taylor, 1997). However, it is known that weak interactions can still play important roles in molecular recognition, self-assembly and other structural processes (MacDonald & Whitesides, 1994).

Each of compounds (II), (III) and (IV) adopts a *trans* planar configuration at the amide (Figs. 1, 2 and 4). However, the nature of the hydrogen bonding present then defines the orientation of the ketone carbonyl group with respect to the amide. In the *ortho*-substituted compound, (II), intramolecular hydrogen bonding between the ketone carbonyl group and the amide N—H group is observed. This serves to give a

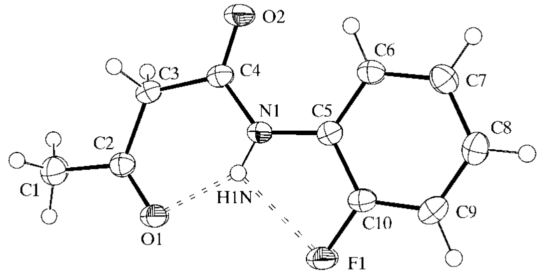


Figure 1
A view of the molecule of (II), showing the atom-numbering scheme and the intramolecular contacts as dashed lines. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

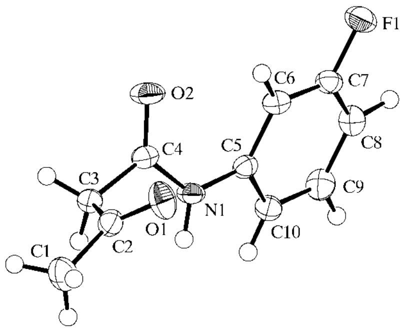


Figure 2
A view of the molecular structure of (III). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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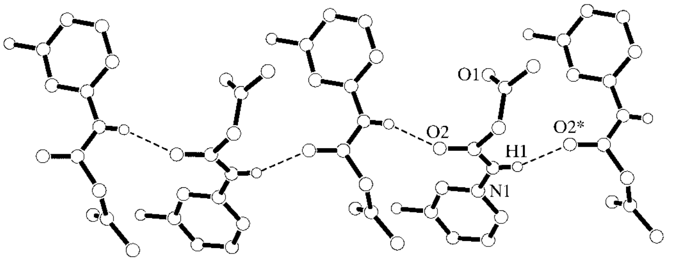

Figure 3
The intermolecular hydrogen bonding in (III), forming a molecular chain that propogates along the *a* direction. The atom labelled with an asterisk (*) is at symmetry position ($x + \frac{1}{2}, y, \frac{1}{2} - z$).

planar arrangement, as shown by the pseudo-torsion angle between the two carbonyl groups [O1—C2···C4—O2 −179.0 (2)°]. The *meta*- and *para*-substituted compounds, however, feature intermolecular hydrogen bonding between N—H and the amide carbonyl group (Fig. 3). Here, the requirement to adopt a planar arrangement is lifted and the equivalent torsion angles are −62.2 (2)° for (III), and −64.0 (2) and −74.8 (2)° for the two independent conformations of (IV). A further difference is that, in (II), the aromatic ring plane is approximately coplanar with the amide plane, whilst both (III) and (IV) exhibit more twisted geometries (see torsion angles in Tables 1, 3 and 5).

Thus, the three compounds are differentiated by the relative conformations of both the aromatic and ketone groups with respect to the amide, and by differences in hydrogen bonding. Similar effects were observed in previous work on methyl-substituted analogues (Chisholm *et al.*, 2000). Therein, we rationalized that a methyl substituent *ortho* to the N—H group sterically disfavoured intermolecular interactions and forced the adoption of a sterically disfavoured planar conformation. That this is a disfavoured strained conformation is shown by a widening of the C2—C3—C4 angle, with values of 122.13 (9) and 122.5 (2)° in, respectively, planar (II) and its methyl analogue, compared with values of 112.6 (2)° for (III), and 110.6 (1) or 110.2 (2)° for (IV). A steric explanation is less likely to be the case with F substitution, due to the similarity in van der Waals radii between H and F. In (II), an explanation may be the high electronegativity of F, which disfavours the approach of the O atom to form an intermolecular hydrogen bond. The coplanarity of the amide group and the aromatic ring is stabilized by an F1···H1N close contact of 2.29 (2) Å. That this is attractive and not incidental may be indicated by the closure of the N1—C5—C10 angle to 117.2 (1)°. We find no evidence of intermolecular H···F interactions in any of these compounds.

In conclusion, the structures presented herein provide further evidence for two broad conformational motifs for acetoacetanilides, namely a planar intramolecular hydrogen-bonded structure and a non-planar intermolecular hydrogen-bonded structure. Which motif is present is dependent on the position of the substituents on the phenyl ring. Whilst the small size of flourine may mitigate against steric effects, its high electronegativity may serve to mimic the effect of a larger group in preventing the close approach of a second molecule to form an intermolecular hydrogen bond.

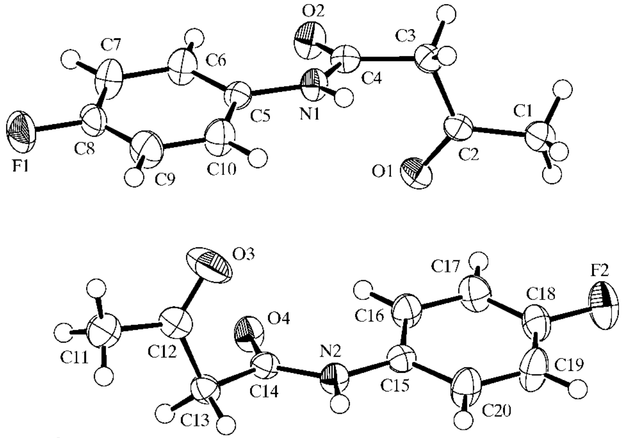

Figure 4
A view of the asymmetric unit of (IV), showing the twisted nature of both crystallographically independent molecules and their atom-numbering schemes. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

Experimental

All starting materials were purchased from Aldrich and used as received, except for xylene (mixture of isomers), which was purified by washing with concentrated sulfuric acid and dried over anhydrous $CaCl_2$. The general synthesis used for the preparation of (II), (III) and (IV) was carried out as follows. A 250 ml three-necked round-bottomed flask was fitted with a magnetic stirrer, a dropping funnel, and a still head and condenser set for downward distillation. To this apparatus were added ethyl acetoacetate (12.9 g, 0.1 mol) and xylene (25 ml). The flask was heated in an oil bath at 420 K with stirring. The appropriate fluorinated aniline (0.09 mol) was then added *via* the dropping funnel and ethanol began to distil. The reaction was continued until the temperature at the still head dropped below the boiling point of ethanol. On cooling to room temperature, off-white crystalline needles formed, which were isolated by filtration and washed with a small amount of petroleum ether (333–353 K), with typical yields of 55–65%. For (II), m.p. 332–334 K; IR spectroscopic data (ν_{max}, nujol, cm^{-1}): 1707 (C═O), 1675 (amide 1), 1620 (aromatic), 1551 (amide 2). For (III), m.p. 339–341 K; IR spectroscopic data (ν_{max}, nujol, cm^{-1}): 1720 (C═O), 1663 (amide 1), 1614 (aromatic), 1548 (amide 2). For (IV), m.p. 364–366 K; IR spectroscopic data (ν_{max}, nujol, cm^{-1}): 1720 (C═O), 1665 (amide 1), 1618 (aromatic), 1552 (amide 2).

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

F1—C10	1.3621 (12)	N1—C4	1.3571 (13)
O1—C2	1.2189 (13)	N1—C5	1.4011 (14)
O2—C4	1.2205 (13)		
C4—N1—C5	128.08 (9)	C10—C5—N1	117.20 (10)
C2—C3—C4	122.13 (9)	C6—C5—N1	125.66 (10)
N1—C4—C3	116.26 (9)	C9—C10—C5	123.35 (10)
C10—C5—C6	117.14 (10)		
O1—C2—C3—C4	2.63 (16)	C4—N1—C5—C10	−176.57 (9)
C5—N1—C4—O2	0.84 (17)	C4—N1—C5—C6	4.27 (17)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O1	0.883 (15)	1.917 (16)	2.6869 (12)	144.7 (13)

Compound (II)

Crystal data

C$_{10}$H$_{10}$FNO$_2$
M_r = 195.19
Monoclinic, $P2_1/c$
a = 7.3215 (2) Å
b = 12.0480 (3) Å
c = 10.5082 (3) Å
β = 98.877 (1)°
V = 915.82 (4) Å^3
Z = 4

D_x = 1.416 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2169 reflections
θ = 1.7–27.5°
μ = 0.11 mm^{-1}
T = 150 (2) K
Cut prism, colourless
0.35 × 0.30 × 0.20 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
3637 measured reflections
2092 independent reflections
1812 reflections with $I > 2\sigma(I)$

$R_{\rm int}$ = 0.015
$\theta_{\rm max}$ = 27.5°
h = 0 → 9
k = −15 → 14
l = −13 → 13

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.094
S = 1.06
2092 reflections
132 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0485P)^2 + 0.2047P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max}$ = 0.23 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.18 e Å^{-3}

Compound (III)

Crystal data

C$_{10}$H$_{10}$FNO$_2$
M_r = 195.19
Orthorhombic, $Pbca$
a = 9.4933 (3) Å
b = 9.7792 (3) Å
c = 20.2345 (7) Å
V = 1878.51 (11) Å^3
Z = 8
D_x = 1.380 Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 2458 reflections
θ = 1.3–27.5°
μ = 0.11 mm^{-1}
T = 150 (2) K
Cut plate, colourless
0.50 × 0.30 × 0.05 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
3999 measured reflections
2158 independent reflections
1387 reflections with $I > 2\sigma(I)$

$R_{\rm int}$ = 0.044
$\theta_{\rm max}$ = 27.5°
h = −12 → 12
k = −12 → 12
l = −26 → 26

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.104
S = 1.02
2158 reflections
167 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F_o^2) + (0.0522P)^2 + 0.0664P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max}$ = 0.18 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.21 e Å^{-3}

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

F1—C7	1.3661 (17)	N1—C4	1.3536 (19)
O1—C2	1.211 (2)	N1—C5	1.4101 (19)
O2—C4	1.2283 (16)		
C4—N1—C5	127.78 (13)	N1—C4—C3	114.63 (13)
C1—C2—C3	115.74 (15)	C8—C7—C6	124.36 (15)
C4—C3—C2	112.62 (14)		
O1—C2—C3—C4	7.5 (2)	C4—N1—C5—C6	24.7 (2)
C5—N1—C4—O2	−4.2 (3)	C4—N1—C5—C10	−156.07 (16)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O2$^{\rm i}$	0.89 (2)	2.05 (2)	2.903 (2)	158.9 (15)

Symmetry code: (i) $\frac{1}{2}+x, y, \frac{1}{2}-z$.

Table 5
Selected geometric parameters (Å, °) for (IV).

F1—C8	1.3655 (19)	O4—C14	1.2304 (18)
F2—C18	1.3685 (19)	N1—C4	1.349 (2)
O1—C2	1.2146 (19)	N1—C5	1.422 (2)
O2—C4	1.2317 (19)	N2—C14	1.350 (2)
O3—C12	1.208 (2)	N2—C15	1.413 (2)
C4—N1—C5	127.60 (14)	C7—C8—C9	122.46 (16)
C14—N2—C15	128.37 (14)	C14—C13—C12	110.15 (13)
C4—C3—C2	110.61 (13)	N2—C14—C13	114.62 (14)
N1—C4—C3	115.21 (14)	C17—C18—C19	122.40 (17)
O1—C2—C3—C4	0.5 (2)	O3—C12—C13—C14	−16.8 (2)
C5—N1—C4—O2	0.7 (3)	C15—N2—C14—O4	1.4 (3)
C2—C3—C4—O2	−81.11 (19)	C12—C13—C14—O4	−75.38 (19)
C4—N1—C5—C6	−14.2 (3)	C14—N2—C15—C16	11.2 (3)
C4—N1—C5—C10	166.01 (16)	C14—N2—C15—C20	−170.91 (16)

Compound (IV)

Crystal data

C$_{10}$H$_{10}$FNO$_2$
M_r = 195.19
Monoclinic, $P2_1/c$
a = 4.9811 (1) Å
b = 20.7383 (4) Å
c = 18.4869 (5) Å
β = 93.021 (1)°
V = 1907.03 (7) Å^3
Z = 8

D_x = 1.360 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4374 reflections
θ = 2.6–27.5°
μ = 0.11 mm^{-1}
T = 150 (2) K
Cut needle, colourless
0.60 × 0.20 × 0.03 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
8284 measured reflections
4372 independent reflections
2728 reflections with $I > 2\sigma(I)$

$R_{\rm int}$ = 0.035
$\theta_{\rm max}$ = 27.5°
h = 0 → 6
k = −26 → 26
l = −23 → 23

Table 6
Hydrogen-bonding geometry (Å, °) for (IV).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1N$\cdots$O4$^{\text{i}}$	0.89 (2)	2.03 (2)	2.914 (2)	172.0 (16)
N2—H2N$\cdots$O2$^{\text{ii}}$	0.88 (2)	1.96 (2)	2.830 (2)	171.2 (18)

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.113$
$S = 1.03$
4372 reflections
263 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 0.3055P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.21$ e Å^{-3}
$\Delta\rho_{\min} = -0.22$ e Å^{-3}

In (III), all H atoms were refined isotropically. However, in both (II) and (IV), only the amide H atom was refined isotropically; all other H atoms were placed in calculated positions, with C—H = 0.95–0.99 Å, and refined in riding modes. The methyl H atoms in (II) were modelled as being rotationally disordered over two sites. The refined N—H distances were 0.872 (19)–0.892 (19) Å and the refined C—H distances were 0.90 (2)–1.018 (17) Å.

For all three compounds, data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Nonius, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1216). Services for accessing these data are described at the back of the journal.

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