Crystal Structure of 1-(3,5-Dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl)urea, an Inhibitor of Chitin Synthesis†

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The crystal structure of 1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl) urea, an inhibitor of chitin synthesis, has been established; the crystal belongs to the triclinic system but with $Z = 6$ and there are three molecules of different conformations in each asymmetric unit; the urea linkage was coplanar for the formation of an intramolecular hydrogen bond.

In contrast to traditional pesticides, benzoyl phenylurea (BPU) and its derivatives mainly controls the growth and development process of insects by interfering with chitin biosynthesis and breeding.[1,2]

Many researchers have studied the quantitative structure–activity relationship (QSAR) of BPU larvicides to analyze the effects of substituents on bioactivity.[3–5] However, owing to the fact that the actual conformation of BPUs and the structure of the acceptor are, as yet, unknown, means that the QSAR is not clear.[3]

In order to determine the structural character and conformation of BPUs, we therefore investigated the crystal structure of a well known BPU, Nomolt,[6,7] by X-ray diffraction (Fig. 1).

According to ref. 7, the title compound was synthesized from 2,3,4,5-tetrachloronitrobenzene and 2,6-difluorobenzamide (Aldrich). It was recrystallized from ethanol, diethyl ether, acetone and DMF, but only DMF gave crystals (mp 223 °C).

It is well known that the high activity of BPUs is attributed to the structure of urea linkage, but it is not clear how it works. The X-ray structure may yield the following explanation. All the atoms of the urea linkage are coplanar (plane 2 in the molecules) to obtain the lowest energy for the formation of an intramolecular hydrogen bond between O(2) and H(2) (1.84 Å). This gives a new conformation for BPUs, and implies that the high bioactivity perhaps is due to the formation of the six-membered ring.

The X-ray structure also showed that there are three molecules (A, B and C) with different conformations in one asymmetric unit (Fig. 2). The differences in conformations mainly relate to dihedral angles between the plane of phenyl (plane 1), the urea linkage (plane 2), and bezoyl (plane 3), which are different in the three molecules (Table 1). This leads to an unusual phenomenon of $Z = 6$ in a triclinic space group.‡

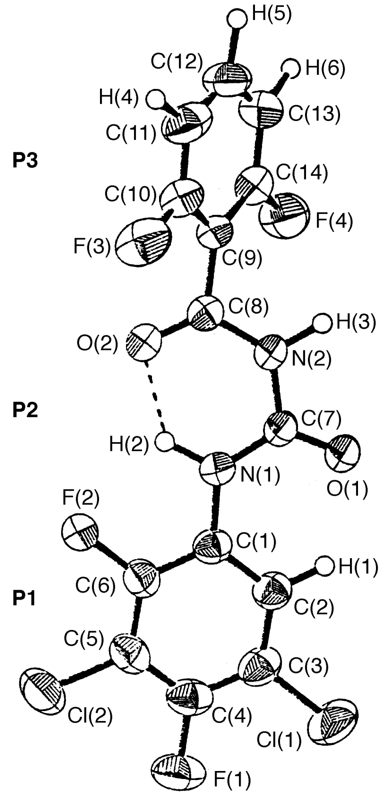

Fig. 1 X-Ray crystal structure of Nomolt

Experimental

Crystal Data for Nomolt.—$C_{14}H_6Cl_2F_4N_2O_2$, $M_r = 381.11$, $F(000) = 380.00$, colorless crystal, triclinic system, $a = 14.380(3)$, $b = 14.587(6)$, $c = 11.837(4)$ Å, $U = 2214(1)$ Å^3, $\alpha = 109.06(2)$, $\beta = 101.88(2)$, $\gamma = 100.26(3)°$, space group $P\bar{1}$, $Z = 6$, $D_c = 1.72$ g cm^{-1}, μ(Mo-Kα) = 5.0 cm^{-1}.§

The intensity data were collected on a Riguku AFC7R diffractometer with Mo-Kα radiation ($\lambda = 0.710\,69$ Å) and ω–2θ scan technique [$T = 293(1)$ K; $0 \leqslant h \leqslant 13$, $-7 \leqslant k \leqslant 14$, $-9 \leqslant l \leqslant 0$; $2\theta_{max} = 45.0$ °].

The structure was solved by direct methods (SHELXS 86)[8] and expanded using Fourier techniques.[9] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

‡The crystal structure described here is very unusual occurring in space group $P\bar{1}$ with 6 molecules per unit cell (normally 2). Running the data through various programs for detecting higher symmetry reveals, only the fairly obvious relationship between molecule B and C in the asymmetric unit *i.e.* a pseudo centre of symmetry (see Fig. 2). The 'centre of symmetry' here is approximately at (0.8, 0.8, 0.5) and as such suggests no particular higher symmetry effect which might be present.

§Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Research (S)*, 1998, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 423/8.

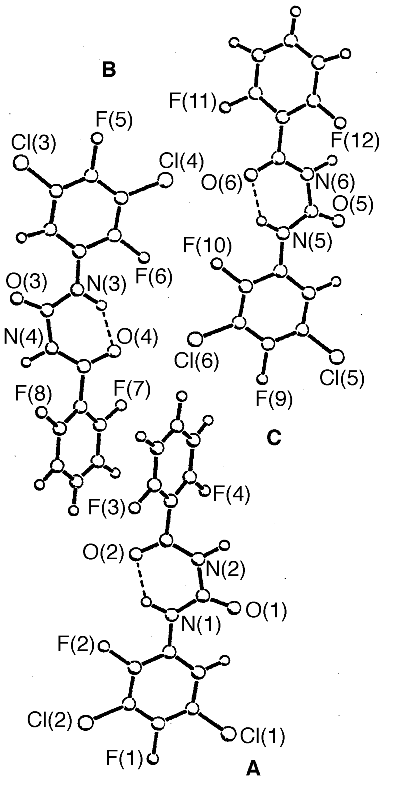

Fig. 2 The structure of asymmetric unit

Table 1 Dihedral angles (°) between planes in molecules **A**–**C**

Molecule	Plane 1–2	Plane 2–3	Plane 1–3
A	168.36	121.43	46.95
B	169.14	128.28	42.69
C	163.76	129.1	34.67

based on 3726 observed reflections [$I > 3.00\sigma(I)$] and 650 variable parameters and converged (largest parameter was 0.01 times its esd) to $R = 0.033$ and $R_w = 0.046$. The weighting scheme, $w = 1/[\sigma^2(F_o)]$ was found to give satisfactory analysis of the variance. The estimated standard deviation for the geometrical parameters involving non-hydrogen atoms lie within the following ranges: bond lengths, 0.003–0.006 Å; bond angles 0.2–0.4°.

Neutral atom scattering factors were taken from Cromer and Waber.[10] Anomalous dispersion effects were included in F_c;[11] values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.[12] The value for the mass attenuation coefficients are those of Creagh and Hubbel.[13] All calculations were performed using the teXsan[14] crystallographic software package of Molecular Structure Corporation.

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