The Crystal Structure of *N*-(5-Phenyl-1,3,4-oxadiazol-2-yl)-*N*′-benzoyl Urea, a Novel Insect-growth Regulator†

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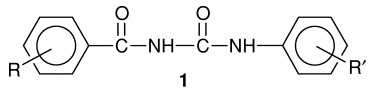
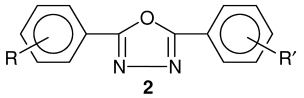
The crystal structure of *N*-(5-phenyl-1,3,4-oxadiazol-2-yl)-*N*′-benzoyl urea, $C_{16}H_{12}N_4O_3$, a novel insect-growth-regulator (IGR), has been established; the crystal structure belongs to the triclinic system with $Z = 2$, and the urea linkage is coplanar with intramolecular hydrogen bond formation, making the structure analogous to a four-ring compound.

In contrast to the traditional pesticides, insect-growth regulators (IGR) mainly control growth and development in insects, especially by regulating chitin biosynthesis, metamorphosis, and breeding.[1,2] Benzoyl phenylurea (BPU) **1** and diaryl oxadiazole (DOZ) **2** are well-known IGRs. Previous research had shown that the urea linkage in BPU and the ring of oxadiazole in DOZ is the biologically active unit.[2]



1



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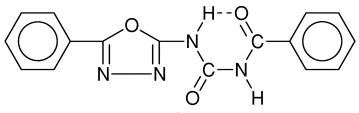


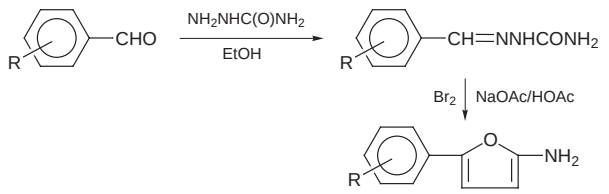
3

As mentioned, BPU and DOZ mainly inhibit chitin synthesis, and the DOZ compounds show high activity in insect biosynthesis: 100 ppm of 2,5-bis(2,4-dichlorophenyl)-1,3,4-oxadiazole, a well known DOZ, was shown to result in up to 50% reduction in the uptake and incorporation of [6-^{3}H]thymidine into DNA in a housefly tissue preparation, and 30% reduction in protein synthesis, while BPU showed no similar effect.[3]

In the study of novel IGRs, we assembled the bioactivity unit of BPU and DOZ to design and synthesize *N*-(5-phenyl-1,3,4-oxadiazol-2-yl)-*N*′-benzoyl urea **3** and its derivatives in order to find a lead compound with high bioactivity as an IGR and inhibitor of DNA and protein synthesis.

The important intermediate, 2-amino-5-aryl-1,3,4-oxadiazole, was synthesized in a two step reaction from substituted benzaldehyde as shown in Scheme 1.[4] The title compound **1** was prepared by reaction of 2-amino-5-phenyl-1,3,4-oxadiazole with benzoyl isocyanate in CH_2ClCH_2Cl. It was recrystallized from DMF to give crystals with mp 212 °C.

We have reported the crystal structure of 1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl)urea,[5] a well known



Scheme 1

BPU, and it shows that the urea linkage is planar with an intramolecular hydrogen bond formed. In order to do further research on quantitative structure-activity relationships (QSAR) of the lead compound, we studied its crystal structure. From the crystal data, we also wanted to find the changes in conformation when the 3,5-dichloro-2,4-difluorophenyl was substituted by 5-phenyl-1,3,4-oxadiazole, and to determine the true conformation of the oxadiazole ring.

From the crystal data, all the atoms of the urea linkage were found to be coplanar giving the lowest energy for the formation of an intramolecular hydrogen bond between O(3) and H(1) (1.87 Å). This makes the title compound similar to a covalent four-ring compound. The conformation obtained will be very valuable in estimating the space factor in the QSAR of the lead compound and the four-ring system may yield an explanation for the compound's limited solubility in nonpolar media.

Crystal Data for Title Compound **3**.—$C_{16}H_{12}N_4O_3$, $M_r = 308.3$, $F(000) = 320$, colorless crystal, triclinic system, $a = 10.041(2)$, $b = 12.292(2)$, $c = 5.819(1)$, $U = 703.693)$ Å^3, $\alpha = 64.61(2)^\circ$, $\beta = 93.17(2)^\circ$, $\gamma = 99.82(2)^\circ$, space group $P\bar{1}$, $Z = 2$, $D_c = 1.455$ g cm^{-3}, μ (Mo–Kα) = 1.04 cm^{-1}.

The intensity data were collected on a Rigaku AFC7R diffractometer with Mo–Kα radiation ($\lambda = 0.710\ 69$ Å) and ω-2θ scan technique [$T = 293(1)$ K; $0 \leqslant h \leqslant 10$, $-14 \leqslant k \leqslant 14$, $-6 \leqslant l \leqslant 6$; $2\theta_{max} = 50.0^\circ$].

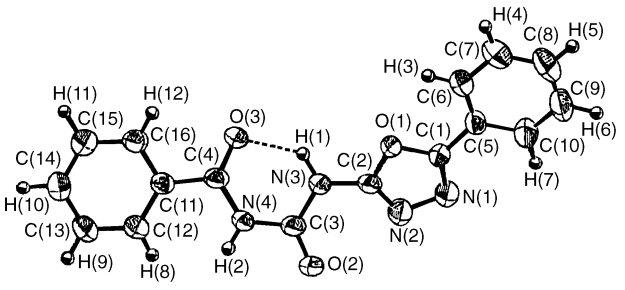


Fig. 1 X-Ray crystal structure of compound **3**

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The structure was solved by direct methods (Fan Hai-Fu)[6] and expanded using Fourier techniques.[7] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement was based on 1649 observed reflections [$I \geqslant 3.00\sigma(I)$] and 257 variable parameters and converged (the largest parameter was $0.01 \times$ esd) to $R = 0.035$ and $R_w = 0.047$. The weighting scheme $w = 1/[\sigma^2(F_o)]$ was found to give a satisfactory analysis of variance. The estimated standard deviations for the geometrical parameters involving non-hydrogen atoms lie within the following ranges: bond lengths, 0.002–0.004 Å; bond angles 0.1–0.2°.

Neutral atom scattering factors were taken from Cromer and Waber[8]. Anomalous dispersion effects were included in F_c;[9] the value of $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.[10] The value for the mass attenuation coefficients are those of Creagh and Hubbel.[11] All calculations were performed using the teXsan[12] crystallographic software package from Molecular Structure Corporation. Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data centre (CCDC). See Instructions for Authors. *J. Chem. Res.* (*S*), 1998, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 423/12.

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