

# Crystal structure of 4-acetyl-1-(4'-fluorophenyl)-5-methyl-2,3-dihydro-1H-pyrrole-2,3-dione verifies the scheme of synthesis

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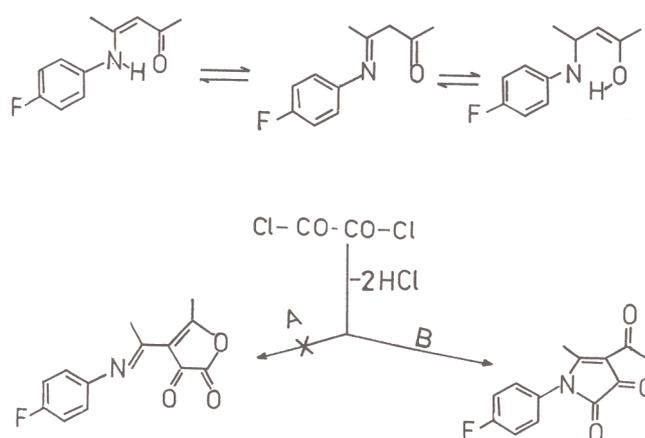
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## Crystal structure / Imaging plate

**Abstract.** The structure of the title compound, crystallized from benzene, in the monoclinic system, space group  $P2_1/c$ , with  $a = 9.032(3) \text{ \AA}$ ,  $b = 10.111(1) \text{ \AA}$ ,  $c = 14.625(1) \text{ \AA}$ ,  $\beta = 121.3(1)^\circ$ ,  $Z = 4$ , has been solved from diffraction data collected on 2D imaging plate detector. This method allowed successful integration of non-uniform reflection profiles with short exposure time. Structural results revealed correct reaction path in the synthesis.

## Introduction

Aiming at the new polycarbonyl heterocycles of potential biological activity the synthesis and pharmacological activity of some 2,3-dihydrofuran-2,3-diones was published [1]. From two possible ways of cyclocondensation of various Schiff bases with oxalyl chloride, corresponding to A or B in Fig. 1, route A was assumed on the basis of chemical evidence and spectral (IR and MS) data. Earlier results [2] suggested, however, the formation of pyrrole-2,3-dione ring in analogous reactions. In view of further ambiguities concerning structure elucidation of nitrogen- and oxygen-containing five-membered heterocycles [3] and wide discussion on this subject in the literature, the present authors decided to prove, by X-ray analysis, the correct reaction pathway and the structure of one reaction product. As an example, the product of the reaction of 4-(4'-fluoroanilino)-4-penten-2-one with oxalyl chloride (Fig. 1) was chosen, especially because it belongs to a whole series of analogous compounds



**Fig. 1.** Alternative schemes of cyclocondensation of *p*-fluoroaniline and acetylacetone Schiff base with oxalyl chloride. Route A suggested by chemical evidence and spectral data was excluded by crystal structure analysis.

showing sedative and analgesic activity in pharmacological tests [1]. Several attempts to crystallize this reaction product using non-polar solvents failed to produce satisfactory crystals. Preliminary diffractometric tests and rotation photographs showed that even low-theta reflections had large reflection width, some of them had non-uniform shape, suggesting anisotropy of mosaicity in some regions of the reciprocal space, and certain reflections were split (cf. Fig. 2), which made it difficult to successfully integrate the reflection profiles using standard diffractometric procedures.

## Experimental

The X-ray diffraction experiment was carried out on a crystal sample of small volume,  $490 \times 10^3 \mu\text{m}^3$ , with reflection width reaching  $1.5^\circ$  at  $\theta = 10^\circ$  ( $\text{CuK}\alpha$ ). Two-

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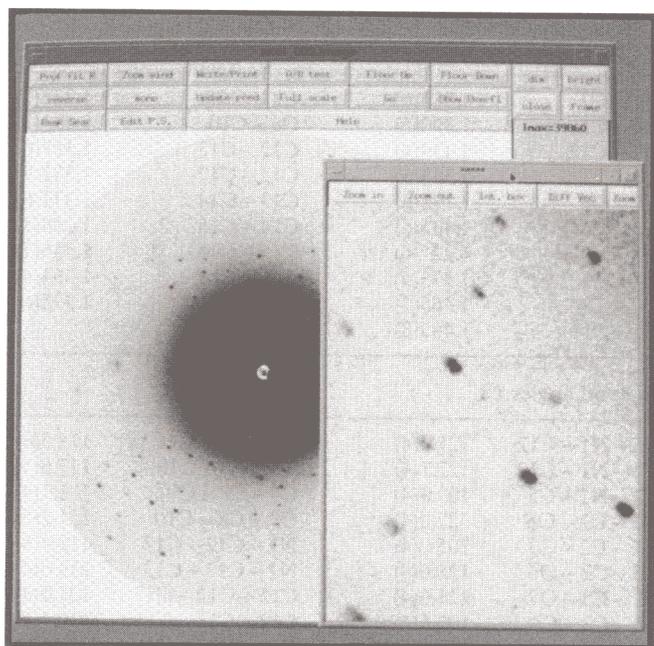


Fig. 2. Diffraction spots with non-uniform mosaicity.

dimensional mapping of reflections on CAD-4 single crystal diffractometer (omega-theta profile plot [4]) confirmed that mosaicity was predominantly responsible for the reflection shape; it turned out, moreover, to be azimuthal angle dependent. Consequently, a search for anisotropy vector was carried out using Duisenberg method [5] for several groups of reflections. For all groups of reflections an agreement between observed and calculated azimuths for the best profiles ( $\psi_o(\text{obs})$  and  $\psi_c(\text{calc})$ ) was within  $5^\circ$ , however, for some of them, e.g. (317) the difference reached  $24^\circ$ . Also, Miller indices calculated for the mosaic anisotropy vector were different for several subsets of reflections, varying from  $(-1.04, 1.00, -1.37)$  to  $(-1.00, 1.09, -2.16)$ . The procedure has been repeated for 24 reflections used for determination of the unit cell parameters. Although the set of reflections with optimized azimuth had about 10% narrower profiles in comparison with those measured at  $\psi = 0$ , but at the same time produced slightly larger standard deviations. Taking into consideration the above results, as well as expected photosensitivity of the sample, a two-dimensional detector was chosen for data collection in order to minimize the exposure time [6, 7, 8].

### Data collection

Mar Research 2D imaging plate detector, 180 mm diameter, single axis phi-rotation method [9],  $\text{MoK}_\alpha$  normal focus X-ray tube, powered at 50 kV, 60 mA, graphite monochromated. The maximum  $2\theta$  was limited by the observed scattering of the crystal sample ( $2\theta = 41.3^\circ$ ). Two sets of data were collected to overcome the limitation of the dynamic range: with crystal-to-plate distance 100 mm and 20 min exposure time (41 images,  $\Delta\phi = 5^\circ$ ), and with crystal-to-plate distance 170 mm and 2 min exposure time (18 images,  $\Delta\phi = 10^\circ$ ). A total of  $180^\circ$  of rotation was recorded for each set. The non-uniform

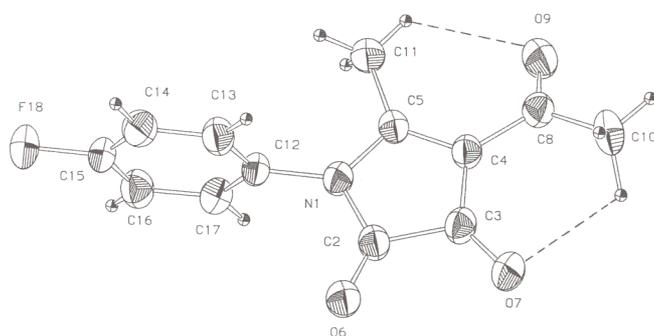


Fig. 3. Perspective drawing of the molecule with the atom numbering scheme. Thermal ellipsoids are plotted at 30% probability. Intramolecular hydrogen bonds are marked by dashed lines.

shape of reflections required the integration box to be rather large to cover complete spot area even in the regions of maximum split.

Data reduction by program DENZO [10]. All 8588 reflections, recorded within 10 h exposure time, were merged to give 1129 unique reflections ( $R_{\text{symm}}(I) = 0.088$ ,  $R_\sigma = 0.056$ ).

The structure was solved by direct methods and difference Fourier syntheses and refined by full-matrix least squares. All hydrogen atoms were found on difference Fourier map and refined (positional, isotropic thermal parameters).

### Results and discussion

$\text{C}_{13}\text{H}_{10}\text{FNO}_3$ ,  $M_r = 243.24$ , monoclinic,  $P2_1/c$ ,  $a = 9.032(3) \text{ \AA}$ ,  $b = 10.111(1) \text{ \AA}$ ,  $c = 14.625(1) \text{ \AA}$ ,  $\beta = 121.3(1)^\circ$ ,  $V = 1146.88 \text{ \AA}^3$ ,  $Z = 4$ ,  $D_x = 1.439 \text{ Mg m}^{-3}$ ,  $\text{MoK}_\alpha$ ,  $\mu = 0.11 \text{ mm}^{-1}$ ,  $F(000) = 512$ ,  $T = 293 \text{ K}$ ,  $R1 = 0.0497$  for 822  $F_o > 4\sigma(F_o)$  and 0.07 for all data,  $wR2 = 0.1371$  for all data,  $S = 1.011$ , Fourier synthesis in  $\text{e}\text{\AA}^{-3}$  max = 0.14, min =  $-0.16$  [11, 12, 13].

A perspective drawing of the molecule with the atom numbering scheme is given in Fig. 3. Fractional atomic coordinates with equivalent thermal parameters are listed in Table 1 and relevant bond lengths and angles are given in Table 2. The molecule consists of two rings: a planar 4'-fluorophenyl ring is rotated by  $88^\circ$  around the N1–C12 bond with respect to the semi-planar (envelope conformation) pyrrole-2,3-dione ring. The C–C bond lengths closest to the F substituent are significantly shorter than other bond distances in the fluorophenyl ring. The corresponding valence angle C14–C15–C16 has the value  $123.6(4)^\circ$ , the largest in the ring. The two carbonyl groups of the latter ring are nearly coplanar with the C2–C3 bond – the corresponding torsional angle equals  $-0.9(9)^\circ$ . The distances and angle involving O9 and C11, H11C atoms from a methyl group (O9...C11 2.994(7)  $\text{\AA}$ , O9...H11C 2.41(5)  $\text{\AA}$ , C11–H11C...O9  $122(4)^\circ$ ) may be interpreted as an intramolecular hydrogen bond. The H11C atom is at a distance of 0.2  $\text{\AA}$  from the C11–C5–O9 plane, which means that it could be moved closer to O9 by a rotation along the C5–C11 bond, but it is not too far from the closest distance allowed by free methyl rotation. Another weak intramolecular

**Table 1.** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ).  $U_{\text{eq}}$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	$U_{\text{eq}}$
N1	6080(4)	-172(3)	3467(2)	59(1)
C2	5821(6)	-957(4)	4148(3)	63(1)
C3	7139(5)	-449(4)	5284(3)	64(1)
C4	8078(5)	592(4)	5140(3)	58(1)
C5	7425(4)	712(4)	4060(3)	54(1)
O6	4792(4)	-1837(3)	3900(1)	79(1)
O7	7219(4)	-938(3)	6072(2)	86(1)
C8	9459(6)	1400(4)	5983(3)	64(1)
O9	10472(4)	2014(3)	5826(2)	83(1)
C10	9594(8)	1437(7)	7044(4)	81(2)
C11	7938(7)	1613(5)	3488(4)	69(1)
C12	5025(5)	-273(4)	2320(3)	54(1)
C13	3517(6)	433(5)	1781(3)	71(1)
C14	2509(6)	325(5)	688(4)	76(1)
C15	3035(6)	-504(5)	182(3)	70(1)
C16	4512(6)	-1228(5)	695(4)	71(1)
C17	5526(6)	-1104(4)	1789(3)	63(1)
F18	2041(3)	-612(3)	-904(2)	104(1)

**Table 2.** Relevant bond lengths and angles.

a) Bond distances ( $\text{\AA}$ )			
N1—C2	1.385(6)	C8—O9	1.222(7)
N1—C5	1.390(5)	C8—C10	1.493(8)
N1—C12	1.439(4)	C12—C13	1.367(6)
C2—C3	1.546(5)	C12—C17	1.372(7)
C2—O6	1.198(6)	C13—C14	1.372(6)
C3—C4	1.435(6)	C14—C15	1.358(8)
C3—O7	1.221(6)	C15—C16	1.356(7)
C4—C5	1.375(5)	C15—F18	1.364(4)
C4—C8	1.465(5)	C16—C17	1.375(6)
C5—C11	1.465(8)		
b) Bond angles ( $^\circ$ )			
C5—N1—C12	127.4(4)	N1—C5—C11	118.5(4)
C2—N1—C12	122.7(4)	C4—C8—C10	117.6(5)
C2—N1—C5	109.9(4)	C4—C8—O9	121.3(4)
N1—C2—O6	127.0(4)	O9—C8—C10	121.2(5)
N1—C2—C3	105.0(4)	N1—C12—C17	119.4(4)
C3—C2—O6	128.0(4)	N1—C12—C13	119.6(4)
C2—C3—O7	121.0(4)	C13—C12—C17	121.0(4)
C2—C3—C4	105.6(4)	C12—C13—C14	119.4(5)
C4—C3—O7	133.4(5)	C13—C14—C15	118.4(5)
C3—C4—C8	126.5(4)	C14—C15—F18	118.7(5)
C3—C4—C5	107.5(4)	C14—C15—C16	123.6(5)
C5—C4—C8	126.0(4)	C16—C15—F18	117.7(5)
N1—C5—C4	111.9(4)	C15—C16—C17	117.7(5)
C4—C5—C11	129.6(4)	C12—C17—C16	119.9(5)

**Table 3.** Intermolecular hydrogen bonds.

D—H...A	D—H [ $\text{\AA}$ ]	D...A [ $\text{\AA}$ ]	H...A [ $\text{\AA}$ ]	D—H...A [ $^\circ$ ]
C10—H10B...O6 <sup>a</sup>	0.94(6)	3.475(8)	2.58(6)	160(4)
C10—H10C...F18 <sup>b</sup>	1.11(8)	3.361(6)	2.51(5)	132(5)
C11—H11B...O6 <sup>c</sup>	0.96(6)	3.433(7)	2.51(7)	161(7)
C14—H14...O9 <sup>d</sup>	0.96(4)	3.323(6)	2.58(5)	134(3)
C16—H16...O6 <sup>e</sup>	0.87(6)	3.388(7)	2.55(6)	163(5)

Equivalent positions:

a:  $-x + 1, -y, -z + 1$

b:  $+x + 1, +y, +z + 1$

c:  $-x + 1, +y + 1/2, -z + 1/2$

d:  $+x - 1, -y + 1/2, +z - 1/2$

e:  $+x, -y - 1/2, +z - 1/2$

hydrogen bond involves O7, C10 and H10C with relevant distances and angle: C10...O7 3.037(7)  $\text{\AA}$ , O7...H10C 2.50(6)  $\text{\AA}$ , C10—H10C...O7 108(4) $^\circ$ . The same hydrogen H10C is at 2.51(5)  $\text{\AA}$  from F18 of the neighboring molecule (C10...F18 3.361(6)  $\text{\AA}$ , C10—H10C...F18 132(5) $^\circ$ ), which may be interpreted as a weak intermolecular hydrogen bond. The molecular packing is determined, moreover, by weak intermolecular hydrogen bonds which involve exposed hydrogens and oxygens (including carbonyl groups), see Table 3<sup>1</sup>.

The crystal structure analysis proved that the reaction of acetylaceton Schiff base with oxalyl chloride leads

to 4-acetyl-1-(4'-fluorophenyl)-5-methyl-2,3-dihydro-1H-pyrrole-2,3-dione (route B in Fig. 1).

This allowed to revise the previous misinterpretation [1] of chemical and spectral data. Unequivocal proof of the molecular structure of the title compound has practical importance, since, according to recent literature data, this heterocyclic system is still a matter of interest being a methylenektene — imidoylketene — oxoketimine precursor [14] and showing, as partly hydrogenated derivative, antiviral activity [15].

The use of a 2D detector for data collection, being a practical alternative for the Duisenberg method, allowed us to perform the integration of partially split reflection profiles and successful refinement of the structure against these intensities.

<sup>1</sup> Additional material to this paper can be ordered referring to the no. CSD 403052, names of the authors and citations of the paper at the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany. The list of  $F_o/F_c$ -data is available from the author up to one year after the publication has appeared.

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