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Instrumental Achievements

Crystal Structure of 3-[2-(4-Pyridyl)]ethyl-6-(2,3-difluorobenzoyl)-2-benzoxazolinone

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Since the first report on the hypnotic properties of 2-benzoxazolinone, a number of derivatives have been tested for various activities, including anticonvulsant, antipyretic, analgesic, cardiotonic, antiulcer, or antibacterial, antimicrobial and antifungal effects. Numerous similar works are currently in progress to obtain a better understanding of the subject; it is clear that choosing a useful starting substance, such as acyl derivatives of benzoxazolinone, is the key step of the medicinal chemistry.

The 6-acylbenzoxazolinones in particular exhibit analgesic properties that are much higher than those of the parent heterocycle, thus allowing the latest developments in the field of central nervous-system drugs. Although electrophilic substitution, such as chlorination, sulfonation and nitration, were achieved using classical reagents, acylation yielding 6-acyl derivatives were found to require particular conditions. The acylation of benzoxazolinone was accomplished earlier by two methods from the literature, in which either DMF-$AlCl_3$ and acid chloride[2] or polyphosphoric and carboxylic acids[1] were used. It was reported that both methods gave the same product (6-acylbenzoxazolinone) and almost the same yields.[3]

The title compound (I) (Fig. 1) was obtained and its structure analyzed by standard analytical techniques (UV, IR, NMR, mass spectroscopy and elemental analysis).[4] In order to obtain information about the stereochemistry of the molecule and to confirm the assigned structure, an x-ray analysis of (I) was undertaken.

6-Acyl-2-benzoxazolinone was obtained by reacting 2-benzoxazolinone with the appropriate carboxylic acid in polyphosphoric acid (PPA).[1] To 2.5 mmol 6-acyl-4-benzoxazolinone was added 7.5 mmol 2-vinylpyridine; the reaction mixture heated under reflux in an oil bath until molten, and then for 2 additional hours at 80˚C. By adding a cold alcohol–water mixture, the product separated; the resulting precipitate was collected by filtration. The crude product was recrystallized from an appropriate solvent.

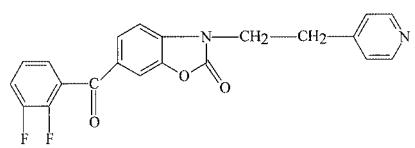

Fig. 1 Chemical structure.

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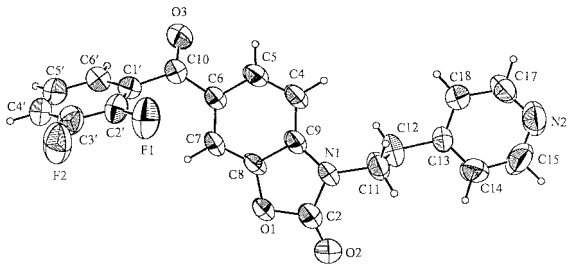

Fig. 2 ORTEP drawing of the title compound with atomic labeling. The displacement ellipsoids are drawn at the 50% probability level.

Table 1 Crystal and experimental data

Formula: $C_{21}H_{14}F_2N_2O_3$	
Formula weight = 380.35	
Crystal system: monoclinic	
Space group: $P2_1/n$	$Z = 4$
a = 6.987(1)Å	
b = 19.806(5)Å	β = 93.28(2)˚
c = 12.745(3)Å	
V = 1760.5(6)Å^3	
D_c = 1.430 g/cm^3	
μ (Mo K_α) = 0.070 mm^{-1}	
T = 295 K	
Orange	
F(0 0 0) = 784	
Crystal size: 0.30 × 0.30 × 0.12 mm	
$2\theta_{max}$ = 52.6˚ with Mo K_α	
R = 0.053	
Rw = 0.056	
No. of reflections used = 1350	($I > 2\sigma(I)$)
No. of parameters = 253	
Goodness-of-fit = 0.91	
$(\Delta/\sigma)_{max}$ = 0.0006	
$(\Delta\rho)_{max}$ = 0.39 eÅ^{-3}	
$(\Delta\rho)_{min}$ = –0.29 eÅ^{-3}	
Measurements: Enraf Nonius CAD-4 diffractometer	
Program system: CAD-4 EXPRESS Software	
Structure determination: MolEN	
Treatment of hydrogen atoms: geometric calculation	
Refinement: full matrix least-squares (MolEN)	

Table 2 Final atomic coordinates and equivalent isotropic thermal parameters for non-hydrogen atoms

Atom	*x*	*y*	*z*	B_{eq}/Å^2
F1	0.5366(4)	0.0250(2)	0.6458(2)	7.94(9)
F2	0.2337(5)	-0.0075(2)	0.5224(2)	8.52(9)
O1	0.6271(4)	0.2330(2)	0.8377(3)	5.05(8)
O2	0.7739(5)	0.3356(2)	0.8547(3)	7.40(9)
O3	0.6433(5)	-0.0630(2)	0.9216(3)	7.70(9)
N1	0.9315(5)	0.2355(2)	0.8970(3)	4.86(9)
N2	1.6982(6)	0.3228(3)	1.1745(4)	7.60(9)
C2	0.7809(7)	0.2764(3)	0.8630(4)	5.40(9)
C4	0.9757(6)	0.1095(2)	0.9156(4)	4.80(9)
C5	0.8748(6)	0.0505(3)	0.9013(4)	4.30(9)
C6	0.6826(6)	0.0489(2)	0.8654(4)	4.50(1)
C7	0.5863(6)	0.1092(2)	0.8400(4)	4.70(9)
C8	0.6883(6)	0.1670(2)	0.8560(4)	4.30(9)
C9	0.8781(6)	0.1687(2)	0.8934(4)	4.40(9)
C10	0.5859(7)	-0.0180(3)	0.8631(4)	5.50(9)
C11	1.1188(6)	0.2621(3)	0.9355(4)	5.10(9)
C12	1.1414(6)	0.2581(3)	1.0537(4)	5.90(9)
C13	1.3376(6)	0.2813(2)	1.0946(4)	4.10(9)
C14	1.3781(7)	0.3476(3)	1.1120(4)	5.70(9)
C15	1.5593(8)	0.3661(3)	1.1515(5)	7.60(9)
C17	1.6575(7)	0.2598(3)	1.1573(4)	6.60(9)
C18	1.4834(7)	0.2359(3)	1.1180(4)	5.50(9)
C1'	0.4135(6)	-0.0317(2)	0.7906(4)	4.60(9)
C2'	0.3986(7)	-0.0109(3)	0.6883(4)	5.00(9)
C3'	0.2418(8)	-0.0298(3)	0.6228(4)	5.50(9)
C4'	0.0971(7)	-0.0667(3)	0.6594(4)	5.60(9)
C5'	0.1082(7)	-0.0871(3)	0.7621(4)	5.70(9)
C6'	0.2659(7)	-0.0704(3)	0.8279(4)	5.40(9)

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* (\boldsymbol{a}_i \cdot \boldsymbol{a}_j)$.

The structure of the molecule is shown in Fig. 2 (ORTEP-MolEN).[2] Table 1 gives the crystal and relevant x-ray data. The fractional coordinates and mean-temperature factors with estimated standard deviations for non-hydrogen atoms are listed in Table 2; selected geometric parameters are given in Table 3.

The benzoxazolinone ring is planar. The dihedral angle between the benzene and oxazolinone ring is 0.8(6)˚. The pyridine ring is also almost parallel to the benzoxazolinone ring with a dihedral angle of 8.5(1)˚. The difluorobenzeyl group at C6 makes a dihedral angle of 63.1(2)˚ with the benzoxazolinone ring, and is bound equatorially. The observed bond lengths, C10–O3 and C2–O2, are normal for a C_{sp^2}=O bond.

Table 3 Selected geometric parameters (Å, ˚)

F1 - C2'	1.338 (6)	O3 - C10	1.216 (6)
F2 - C3'	1.351 (6)	C11- C12	1.507 (6)
N1 - C2	1.378 (6)	O2 - C2	1.179 (6)
N1 - C11	1.469 (6)	C8 - C9	1.384 (6)
O1 - C2	1.399 (6)	N2 - C15	1.316 (7)
O1-C2-O2	124.2 (4)	C6-C10-C1'	121.4 (4)
N1-C11-C12	110.8 (4)	F1-C2'-C1'	122.0 (4)
C11-C12-C13	111.7 (4)	F2-C3'-C4'	120.8 (5)
C6-C10-O3	120.5 (4)		
N1-C11-C12-C13	176.6 (4)	C11-C12-C13-C14	84.6 (6)
C6-C10-C1'-C6'	-140.8 (5)	N1-C9-C4-C5	179.0 (5)
C2-N1-C11-C12	103.7 (5)		

Table 4 Hydrogen bond geometry

D–H···A	D···A	D–H	H···A	<D–H···A
C5-H5...O3	2.790 (7)	0.946	2.502	97.6
C10-H10a...02	2.950 (6)	0.954	2.616	100.9

Geometric details of the hydrogen bonds are given in Table 4. There are two intra-molecular C–H··O hydrogen bonds, among which that between H11a and O2 contributes to the planarity of the molecule as a whole.

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