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Diethyl 1-(4-fluorophenyl)-3-(2-furyl)-5-oxopyrrolidine-2,2-dicarboxylate and diethyl 1-(3,4-dichlorophenyl)-3-(2-furyl)-5-oxopyrrolidine-2,2-dicarboxylate

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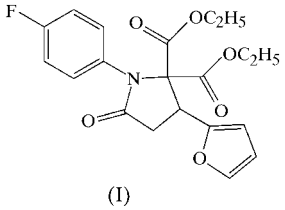
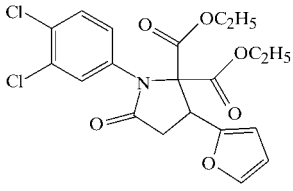
The title compounds, $C_{20}H_{20}FNO_6$ and $C_{20}H_{19}Cl_2NO_6$, respectively, may exhibit bioactivity. In these compounds, the pyrrolidine ring adopts a conformation intermediate between envelope and half-chair. Only one of the two ethoxycarbonyl side chains is nearly planar. Centrosymmetric pairs are formed, and the crystal structure is stabilized by weak C—H···O hydrogen bonds and van der Waals interactions.

Comment

Bioactivity of lactam compounds depends on their ability to acylate several proteins to inhibit the crosslinking of bacterial cell walls (Baldwin *et al.*, 1991), which in turn is dependent on the presence of a suitably substituted and activated lactam ring (Baldwin *et al.*, 1984). It has been observed that *N*-phenyl-γ-lactam derivatives exhibit gram-positive and gram-negative antibacterial activities, and the replacement of the phenyl group by a 2-furyl moiety at the 4-position of the γ-lactam ring causes this compound to be moderately active (Ray *et al.*, 1994). In the variation of *N*-aryl substituents, the replacement of the *N*-phenyl by the *N*-4-chlorophenyl group increased the antibacterial activity significantly (Kar *et al.*, 1998). It has also been found that the introduction of fluorine into the aryl moiety alters the activity of many organic compounds abnormally, by affecting the half-life of the drug. The title compounds, (I) and (II), were synthesized in order to obtain novel γ-lactam analogues with potential bioactivity. The crystal structure determinations of (I) and (II) were carried out in order to elucidate their molecular conformations.



(I)



(II)

Both compounds contain one phenyl ring (C5–C10), one furan ring (C11–C14/O2) and one pyrrolidine ring (C1–C4/N1; Figs. 1 and 2). The pyrrolidine ring is intermediate between envelope and half-chair conformations, with a local pesudo-mirror running through atom C3 and the mid-point of the C1—N1 bond, and a local pseudo-twofold axis running through atom C1 and the mid-point of the C3—C4 bond (Duax *et al.*, 1976). Atom C3 deviates from the mean plane passing through the remaining atoms in the ring by 0.476 (3) Å in (I) and 0.492 (3) Å in (II). The conformation of the pyrrolidine ring is dictated by the existence of intramolecular

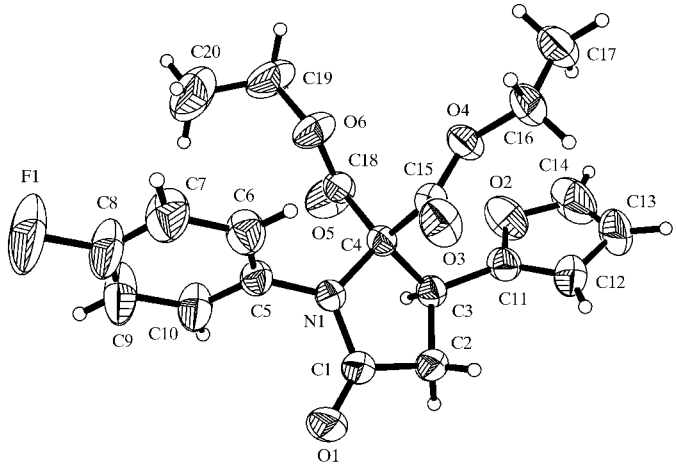


Figure 1
A view of (I), showing the atomic numbering scheme and 50% probability displacement ellipsoids.

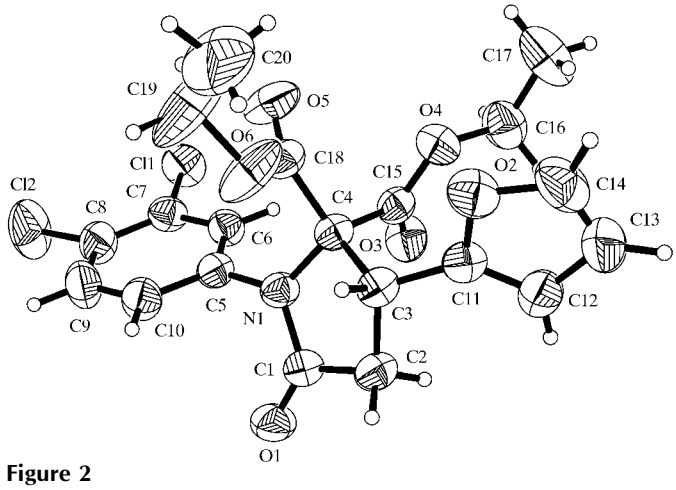


Figure 2
A view of (II), showing the atomic numbering scheme and 50% probability displacement ellipsoids.

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contacts [C11···O4 = 2.878 (2) Å in (I) and 2.876 (3) Å in (II)]. The distortion of the pyrrolidine ring also affects the N1—C4—C3 ring angle [101.46 (12)° in (I) and 100.97 (16)° in (II)]. The plane of the phenyl group is twisted from the plane of the furan ring by 74.01 (7) and 84.46 (9)° in (I) and (II), respectively. The dihedral angle between the phenyl and pyrrolidine rings is 69.79 (8)° in (I) and 64.05 (8)° in (II), and the angle between the pyrrolidine and furan rings is 56.42 (10)° in (I) and 46.38 (12)° in (II).

In both compounds, one of the ethyl acetate chains is completely extended, with all of the non-H atoms coplanar [the mean deviation from the C4/C15/O3/O4/C16/C17 plane is 0.060 (1) Å for (I) and 0.050 (1) Å for (II)]. The other ethyl acetate chain is twisted, the C18—O6—C19—C20 torsion angle being 96.1 (2)° for (I) and −116.5 (5)° for (II). In this chain in (II), a weak attractive intramolecular contact (O6···H3*A* = 2.35 Å) is found. Slight disorder, which is more marked in (II), is also apparent at the end of the twisted ethyl acetate chain (C19/C20), as evidenced by the U_{eq} values and the short C19—C20 distance [1.390 (6) Å for (II); Table 3].

The C11—C12 and C13—C14 distances (Tables 1 and 3) confirm the double-bond character of these linkages. These distances are shorter than those found in the related compounds in which a thiophene ring replaces the furan ring [(I): Usman *et al.*, 2001; (II): Ray *et al.*, 1998]. In both compounds, the intermolecular interaction between atoms H14*A* and O1 shortens the nearest C═C double bond in the furan ring [C13═C14 = 1.309 (4) Å in (I) and 1.316 (5) Å in (II)]. The presence of the F atom in (I) causes a shortening of the nearest C—C bonds [C7—C8 = 1.351 (3) Å and C8—C9 = 1.361 (3) Å]. On the other hand, a short intermolecular contact between atoms Cl1 and O5 [Cl1···O5 = 3.164 (2) Å] is found in (II). In both compounds, centrosymmetric pairs are formed. As has been found in related compounds, weak hydrogen bonds (Tables 2 and 4) and van der Waals interactions stabilize the crystal structures (Figs. 3 and 4)

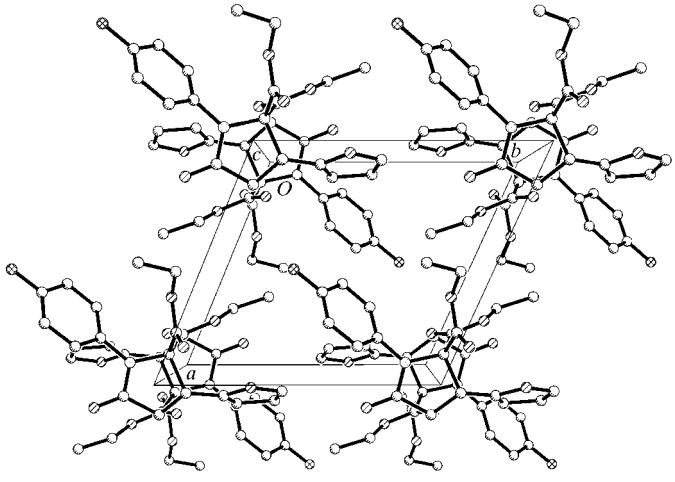

Figure 3
A packing diagram of (I), viewed along the *c* axis. H atoms have been omitted for clarity.

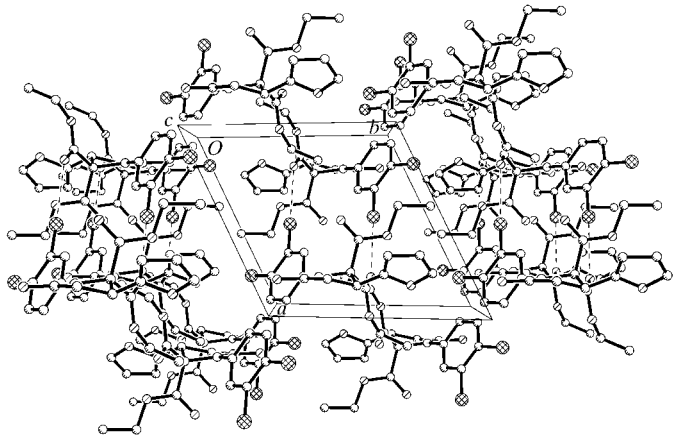

Figure 4
A packing diagram of (II), viewed along the *c* axis. H atoms have been omitted for clarity.

Experimental

The title compounds were synthesized *via* an intermolecular Michael addition reaction, followed by an intramolecular amidification reaction, between diethyl 4-fluoro/3,4-dichloroanilinomalonate (synthesized by the condensation reaction between substituted aniline and diethyl bromomalonate) and 3-(2-furyl)acryloyl chloride in the presence of triethylamine, using dry benzene as solvent. Single crystals were grown by slow evaporation at room temperature of a solution of the resulting compound in 2-propanol. Compound (I): colourless solid; m.p. 355–357 K (2-propanol); ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.92–1.24 (*m*, 6H), 2.80–3.13 (*dd*, 2H, *J* = 8.8, 16.7 Hz), 3.74–3.86 (*m*, 1H), 3.91–4.17 (*m*, 3H), 4.61–4.71 (*dd*, 1H, *J* = 8.7, 11.3 Hz), 6.28–6.35 (*m*, 2H), 7.01–7.09 (*m*, 1H), 7.21–7.28 (*m*, 3H), 7.37–7.38 (*d*, 1H, *J* = 1.31 Hz). Compound (II): colourless solid; m.p. 353–355 K (2-propanol); ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99–1.06 (*t*, 6H, *J* = 7.1 Hz), 2.82–3.12 (*dd*, 2H, *J* = 8.8, 16.7 Hz), 3.73–3.85 (*m*, 1H), 3.98–4.20 (*m*, 3H), 4.57–4.67 (*dd*, 1H, *J* = 8.8, 10.8 Hz), 6.28–6.36 (*m*, 2H), 7.12–7.17 (*dd*, 1H, *J* = 2.4, 8.6 Hz), 7.38–7.46 (*m*, 3H).

Compound (I)

Crystal data

$C_{20}H_{20}FNO_6$
M_r = 389.37
Triclinic, $P\overline{1}$
a = 9.582 (3) Å
b = 10.157 (3) Å
c = 11.384 (4) Å
α = 90.305 (6)°
β = 105.358 (6)°
γ = 112.405 (5)°
V = 980.6 (5) Å^3
Z = 2
D_x = 1.319 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 2470 reflections
θ = 2.0–28.0°
μ = 0.10 mm^{-1}
T = 293 (2) K
Block, colourless
0.39 × 0.36 × 0.22 mm

Data collection

Siemens SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: empirical (*SADABS*; Sheldrick, 1996)
T_{min} = 0.885, T_{max} = 0.978
6019 measured reflections
4167 independent reflections
2936 reflections with $I > 2\sigma(I)$
R_{int} = 0.015
θ_{max} = 27.0°
h = −12 → 12
k = −12 → 12
l = −14 → 11

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0644P)^2 + 0.1569P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.046$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.130$	$\Delta\rho_{max} = 0.22$ e Å^{-3}
$S = 1.03$	$\Delta\rho_{min} = -0.25$ e Å^{-3}
4167 reflections	
255 parameters	
H-atom parameters constrained	

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

C7—C8	1.351 (3)	C13—C14	1.309 (4)
C8—C9	1.361 (3)	C19—C20	1.463 (4)
C11—C12	1.333 (3)		
N1—C4—C3	101.46 (12)		
C1—N1—C5—C10	−66.6 (2)	C19—O6—C18—C4	−176.75 (16)
C16—O4—C15—C4	−167.98 (14)	C18—O6—C19—C20	96.1 (2)
C15—O4—C16—C17	177.24 (15)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2B···O3^{i}	0.97	2.49	3.457 (2)	174
C14—H14A···O1^{ii}	0.93	2.43	3.220 (3)	143
C19—H19A···O1^{iii}	0.97	2.60	3.410 (3)	141

Symmetry codes: (i) $-x, 2-y, 1-z$; (ii) $x, y-1, z$; (iii) $1+x, y, z$.

Compound (II)

Crystal data

$C_{20}H_{19}Cl_2NO_6$	$Z = 2$
$M_r = 440.26$	$D_x = 1.394$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 9.5478$ (9) Å	Cell parameters from 2877 reflections
$b = 10.2319$ (9) Å	$\theta = 2.0$–$28.0°$
$c = 12.5088$ (11) Å	$\mu = 0.35$ mm^{-1}
$\alpha = 72.749$ (2)°	$T = 298$ (2) K
$\beta = 86.206$ (2)°	Block, colourless
$\gamma = 64.310$ (2)°	0.23 × 0.19 × 0.15 mm
$V = 1048.91$ (16) Å^3	

Data collection

Siemens SMART CCD area-detector diffractometer	3184 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.018$
φ and ω scans	$\theta_{max} = 27.0°$
Absorption correction: empirical (*SADABS*; Sheldrick, 1996)	$h = -12 \rightarrow 12$
	$k = -13 \rightarrow 7$
$T_{min} = 0.875$, $T_{max} = 0.950$	$l = -15 \rightarrow 15$
6438 measured reflections	
4450 independent reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0601P)^2 + 0.4142P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.048$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.140$	$\Delta\rho_{max} = 0.37$ e Å^{-3}
$S = 1.05$	$\Delta\rho_{min} = -0.41$ e Å^{-3}
4450 reflections	
264 parameters	
H-atom parameters constrained	

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

C7—C8	1.384 (3)	C13—C14	1.316 (5)
C8—C9	1.382 (4)	C19—C20	1.390 (6)
C11—C12	1.334 (4)		
N1—C4—C3	100.97 (16)		
C1—N1—C5—C10	62.2 (3)	C19—O6—C18—C4	−173.7 (3)
C16—O4—C15—C4	169.97 (19)	C18—O6—C19—C20	−116.5 (5)
C15—O4—C16—C17	−178.4 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2A···O3^{iv}	0.97	2.43	3.355 (3)	159

Symmetry code: (iv) $1-x, 1-y, -z$.

All H atoms were placed geometrically and treated as riding on their parent atoms, with aromatic C—H distances of 0.93 Å, methylene C—H distances of 0.97 Å and methyl C—H distances of 0.96 Å. The U_{iso}(H) values were set at $1.5U_{eq}$(C) for the methyl H atoms and at $1.2U_{eq}$(C) for the other C-bound H atoms.

For both compounds, data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 1997); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1631). Services for accessing these data are described at the back of the journal.

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