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1-Substituted derivatives of 2-phenylpyrrolidine-2-carboxamide

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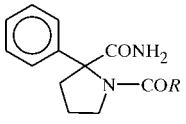
The structures of two potential anti-human immunodeficiency virus type 1 (HIV-1) non-nucleoside reverse transcriptase inhibitors (NNRTI), namely 1-(2-chlorobenzoyl)-2-phenylpyrrolidine-2-carboxamide, $C_{18}H_{17}ClN_2O_2$, and 1-(2-furoyl)-2-phenylpyrrolidine-2-carboxamide, $C_{16}H_{16}N_2O_3$, have been investigated by X-ray diffraction and the butterfly-like conformation established in each case. The pyrrolidine ring has the same half-chair conformation in both structures.

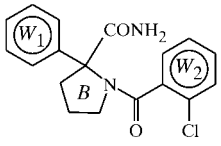
Comment

We are currently investigating compounds belonging to the family of non-nucleoside reverse transcriptase inhibitors (NNRTIs). Formally, the structures of such compounds may be considered as derivatives of loviride (Pauvels *et al.*, 1993), with the common structural feature being the butterfly-like conformation (De Clercq, 1996). A new method for the

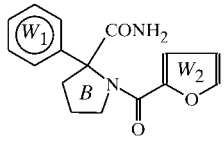


R = alkyl or aryl

(I)



(II)



(III)

synthesis of 1,2-substituted derivatives of 1-(alkyl/arylcarbonyl)-2-phenylpyrrolidine-2-carboxamide, (I), has been developed by Martirosyan *et al.* (2000), and thus 1-(2-chlorobenzoyl)-2-phenylpyrrolidine-2-carboxamide, (II), and 1-(2-furoyl)-2-phenylpyrrolidine-2-carboxamide, (III), have been synthesized as racemic mixtures. The crystal structures of these two compounds are presented here.

Views of molecules (II) and (III) with the atomic numbering schemes are shown in Figs. 1 and 2, respectively. In the crystal structures of both compounds, two neighbouring asymmetric molecules, related by inversion centres, are connected into a dimeric unit *via* double hydrogen bonds involving the amide groups (Figs. 3 and 4). However, only one of the amide H atoms of each molecule [H15*A* in (II) and H14*A* in (III)] takes part in the dimer formed through intermolecular interactions. The other H atoms (H15*B* and H14*B*, respectively) of the amide form intramolecular hydrogen bonds with the carbonyl O7 atoms.

The interatomic distances and angles for the hydrogen bonds in (II) and (III) are listed in Tables 1 and 2, respectively. The formation of intramolecular hydrogen bonds in (II) and (III) could bring additional rigidity to the molecular conformation relative to 1-benzyl-5-oxo-2-phenylpyrrolidine-2-carboxamide (Karapetyan *et al.*, 2002), in which the corresponding H atoms take part in intermolecular bonding.

The dihedral angles between the aryl groups ('wing' planes W_1 and W_2 in the *Scheme*) and the pyrrolidine ring (part of the 'body', plane *B* in the *Scheme*), describing the orientation relations between the 'wings' and 'bodies' of these butterfly-like structures, for planes W_1/W_2, B/W_1 and B/W_2 are 40.05 (12), 72.02 (10) and 86.69 (10)°, respectively, for (II), and 89.99 (7), 76.69 (6) and 29.04 (10)°, respectively, for (III). The differences in these dihedral angles are caused by the reorientation of plane W_2. Probably, in this reorientation, the

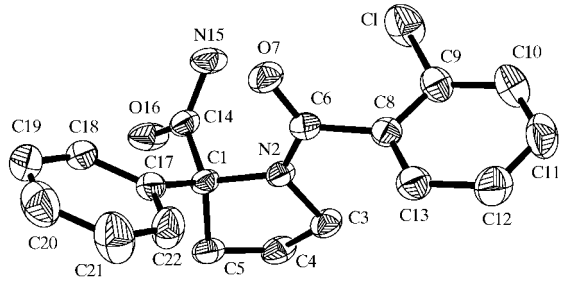


Figure 1
A view of (II) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted for clarity.

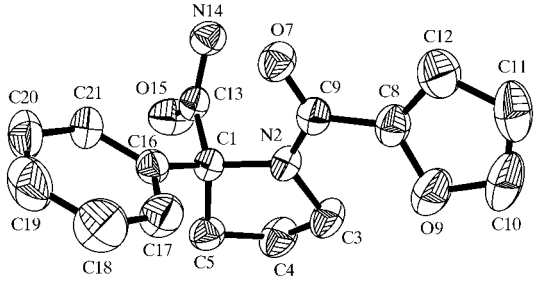


Figure 2
A view of (III) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted for clarity.

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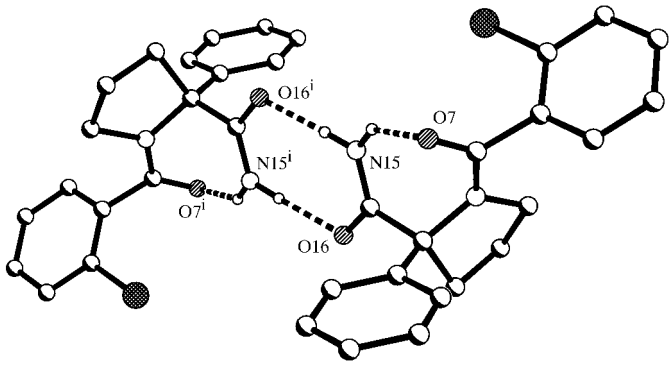

Figure 3
The connection of molecules of (II) into dimers [symmetry code: (i) $2-x$, $1-y$, $2-z$].

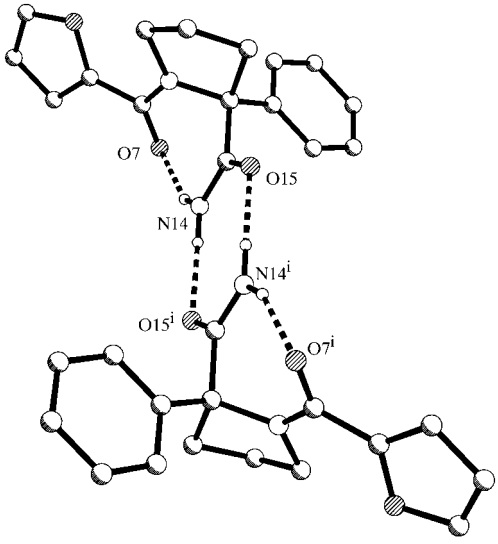

Figure 4
The connection of molecules of (III) into dimers [symmetry code: (i) $1-x$, $2-y$, $2-z$].

essential role played by the Cl atom in the *ortho*-position of the phenyl ring is prominent. In both structures, the pyrrolidine ring has the same half-chair conformation.

Experimental

The title compounds, (II) and (III), were synthesized as described by Martirosyan *et al.* (2000). In each case, recrystallization from ethanol afforded colourless crystals suitable for X-ray analysis.

Compound (II)

Crystal data

$C_{18}H_{17}ClN_2O_2$
M_r = 328.79
Monoclinic, $P2_1/c$
a = 10.661 (2) Å
b = 11.690 (2) Å
c = 20.698 (4) Å
β = 138.60 (3)°
V = 1706.1 (11) Å^3
Z = 4
D_x = 1.280 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 22 reflections
θ = 13.9–20.0°
μ = 0.23 mm^{-1}
T = 293 (2) K
Prism, colourless
0.20 × 0.13 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
3296 measured reflections
2948 independent reflections
1928 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
θ_{max} = 25°
$h = -12 \rightarrow 11$
$k = 0 \rightarrow 13$
$l = -11 \rightarrow 24$
3 standard reflections
frequency: 60 min
intensity variation: ±1.0%

Refinement

Refinement on F^2
$R(F)$ = 0.048
$wR(F^2)$ = 0.148
S = 0.95
2948 reflections
208 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0453P)^2 + 0.4186P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

Table 1
Short N—H···O contacts (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N15—H15B···O7	0.86	2.099	2.851 (2)	146
N15—H15A···O16^{i}	0.86	2.007	2.865 (2)	175

Symmetry code: (i) $2-x$, $1-y$, $2-z$.

Compound (III)

Crystal data

$C_{16}H_{16}N_2O_3$
M_r = 284.31
Monoclinic, $P2_1/c$
a = 12.665 (3) Å
b = 12.214 (2) Å
c = 9.3453 (19) Å
β = 91.98 (3)°
V = 1444.8 (5) Å^3
Z = 4
D_x = 1.307 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 22 reflections
θ = 17.7–23.2°
μ = 0.09 mm^{-1}
T = 293 (2) K
Prism, colourless
0.26 × 0.16 × 0.14 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
2652 measured reflections
2533 independent reflections
2185 reflections with $I > 2\sigma(I)$
R_{int} = 0.012
θ_{max} = 25°
$h = 0 \rightarrow 15$
$k = -14 \rightarrow 0$
$l = -11 \rightarrow 11$
3 standard reflections
frequency: 60 min
intensity variation: ±1.0%

Refinement

Refinement on F^2
$R(F)$ = 0.037
$wR(F^2)$ = 0.125
S = 1.01
2533 reflections
191 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0453P)^2 + 0.4186P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.081 (6)

Table 2
Short N—H···O contacts (Å, °) for (III).

D—H···A	D—H	H···A	D···A	D—H···A
N14—H14A···O15^{i}	0.86	2.070	2.919 (2)	169
N14—H14B···O7	0.86	1.985	2.768 (2)	151

Symmetry code: (i) $1-x$, $2-y$, $2-z$.

Compounds (II) and (III) crystallized in the monoclinic system, space group $P2_1/c$, as determined from the systematic absences. H

atoms were constrained, with C—H distances in the range 0.93–0.97 Å and N—H distances of 0.86 Å.

For both compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *SETANG* in *CAD*-4 *Software*; data reduction: local program; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1113). Services for accessing these data are described at the back of the journal.

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