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N-[1-(Pentafluorophenyl)ethyl]-acetamide

Ilia A. Guzei,* Benjamin C. Gorske and Helen E. Blackwell

Department of Chemistry, University of Wisconsin–Madison, 1101 University Avenue, Madison, WI 53706, USA
Correspondence e-mail: iguzei@chem.wisc.edu

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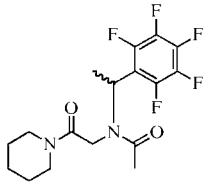
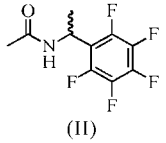
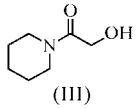
The title compound, $C_{10}H_8F_5NO$, crystallizes as a racemate with four symmetry-independent molecules in the asymmetric unit. The four molecules form two hydrogen-bonded pairs. Each pair is a building unit of an independent $C(4)$ chain propagating parallel to the *ab* plane.

Comment

We are interested in examining the folding propensities of *N*-substituted glycine oligomers, or 'peptoids', a class of peptidomimetics with interesting structural and biological properties (Simon *et al.*, 1992). In the course of our investigations, we sought to synthesize peptoids containing α-chiral fluoroaromatic side chains in order to explore π–π stacking interactions in peptoid helices (Gorske *et al.*, 2005; Kirshenbaum *et al.*, 1998; Wu *et al.*, 2001). We designed a monomeric system, (I), to determine how this side-chain affects conformational behavior. A mixture of products was obtained from the solution-phase synthesis of compound (I). Purification by silica-gel chromatography using ethyl acetate as the eluent afforded the desired product and a mixture of by-products (R_F = 0.6). NMR analysis of the by-products in $CDCl_3$ (300 MHz) suggested that the mixture consisted of compounds (II) and (III) in an approximate 3:2 ratio. The mixture was dissolved in 1:1 *n*-heptane–chloroform and the solution allowed to evaporate at room temperature, yielding colorless crystals, which proved to contain only the title compound, (II), in the form of a racemate in the centrosymmetric triclinic space group $P\overline{1}$.


(I)


(II)


(III)

The asymmetric unit of (II) contains four independent molecules (*A*–*D*) with the same configuration of the stereogenic center C3 (Fig. 1). The Cambridge Structural Database (CSD; Version 5.27, update of January 2006; Allen, 2002) contains 652 structures (0.18%) with $Z = 8$ and $Z' = 4$, of which 203 organic and 135 organometallic compounds crystallize in the space group $P\overline{1}$. Examples include 4-methyl-3-nitroaniline, which forms molecular $R_4^3(18)$ ladders (Cannon *et al.*, 2001), maleimide, which forms discrete $R_2^2(8)$ dimers in the solid state (Cox & Parker, 1996), and 5-nitro-2,4-dihydro-1,2,4-triazol-3-

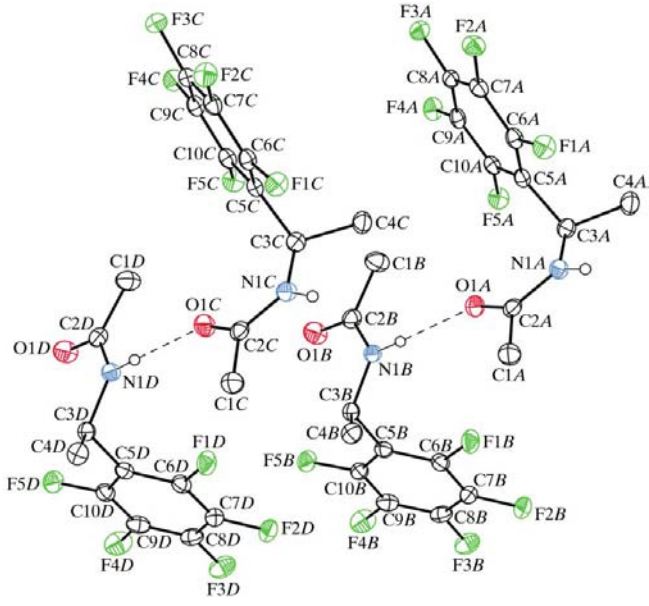


Figure 1
The molecular structure of (II), showing the four symmetry-independent molecules (suffixes *A*–*D*). Displacement ellipsoids are drawn at the 50% probability level. All H atoms, except the amide NH atoms, have been omitted for clarity. Hydrogen-bonding interactions are shown as dashed lines.

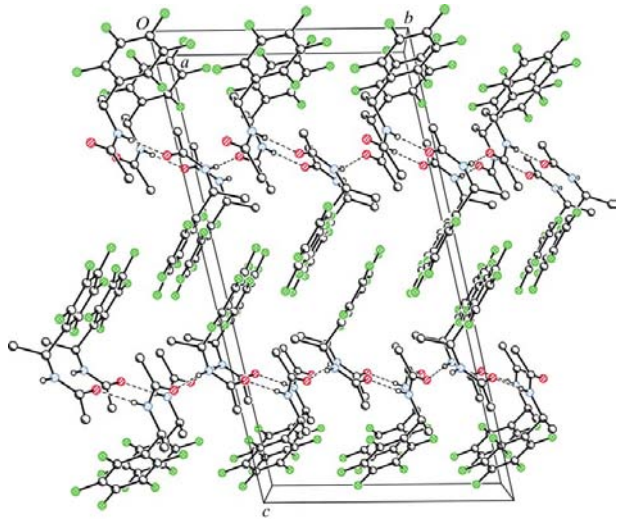


Figure 2
A packing diagram of (II), viewed along the *a* axis. All H atoms, except the amide NH atoms, have been omitted for clarity. Hydrogen-bonding interactions are shown as dashed lines.

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one, which crystallizes as a four-component twin (Bolotina *et al.*, 2005).

In the asymmetric unit of (II), the molecules are positioned pairwise with intermolecular N—H···O hydrogen bonds between molecules *A* and *B* and between molecules *C* and *D* (Fig. 1). The donor–acceptor N···O separations fall in the range 2.8380 (15)–2.8855 (15) Å, with N—H···O angles between 156 and 172°. These relatively strong hydrogen bonds are thought to be the driving force for the crystallization of (II).

The hydrogen-bonding motif in (II) is *C*(4) (Bernstein *et al.*, 1995) in all cases. The parallel hydrogen-bonded chains of the same chiral configuration propagate in the [120] direction and are stacked in planes with alternating chiral configurations along the crystallographic *c* axis. While there are no interchain hydrogen bonds, there is a number of F···F contacts that are shorter than the sum of the F 'zero-point energy' radius of 2.826 Å, defined as the distance at which the F···F interactions become predominantly repulsive (Guzei & Wendt, 2006). The contacts are between chains *A* and $A(1+x, y, z)$, *A* and $C(2-x, -y, 1-z)$, *A* and $C(1-x, -y, 1-z)$, *B* and $D(x, 1+y, z)$, and *C* and $C(1+x, y, z)$, with the shortest distance being 2.7722 (11) Å between atoms F3*A* and F4$C(1-x, -y, 1-z)$. The energy required to reposition two F atoms from 2.826 to 2.772 Å has been estimated with a Morse potential and found to be ∼0.04 kcal mol^{-1} (1 kcal mol^{-1} = 4.184 kJ mol^{-1}).

Interestingly, molecules *B* and *D* have similar geometries, while those of *A* and *C* are noticeably different. Thus, two different hydrogen-bonded chains are present. It is important to compare Figs. 2 and 3. The lattice content viewed along the *a* axis (Fig. 2) seems to reveal a regular packing pattern. However, the lattice perspective examined along the *b* axis (Fig. 3) shows that molecules *B* and *D* at the short *a*-axis edges of the lattice are in more similar conformations than molecules *A* and *C*, with the offset pentafluorophenyl rings in the middle of the unit cell. A closer inspection of the molecular conformations reveals that all four molecules differ: torsion angles N1—C3—C5—C6 in molecules *A*–*D* and in the molecule of (II) with its geometry optimized at the pbe1pbe/6-31+G* level of theory (II-DFT) (*GAUSSIAN03*; Frisch *et al.*, 2004) are 55.23 (17), 64.47 (16), 47.80 (16), 66.39 (16) and 52.3°, respectively. A somewhat smaller variation is observed for torsion angles C2—N1—C3—C5 for the five molecules in the same order: 74.23 (14), 87.95 (15), 81.32 (15), 84.22 (15) and 89.0°.

The average C—F bond length of 1.341 (3) Å for molecules *A*–*D* is statistically equivalent to the corresponding averaged distance in (II-DFT) [1.334 (6) Å]. A scrutiny of the amide link shows that the delocalization of electron density in the planar H—N—C═O unit due to the n(N1)→π^*(C2═O1) donation is more prominent in the experimental data [N1—C2 = 1.340 (3) Å and C2═O1 = 1.232 (2) Å] than in the theoretical model (N1—C2 = 1.37 Å and C2═O1 = 1.22 Å), where the differences are statistically significant. This may in part be attributed to the intermolecular hydrogen bonding, which would elongate the experimentally observed C═O double bonds relative to that in the theoretical model, in which intermolecular effects were absent. A natural bond-orbital analysis of (II-DFT) computed the bond orders for bonds N1—C2 and C2═O1 to be 1.1 and 1.9, respectively.

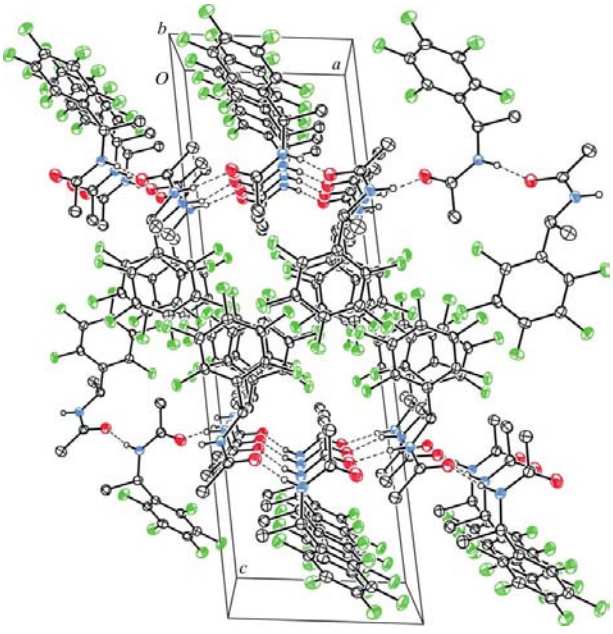

Figure 3
A packing diagram of (II), viewed along the *b* axis. All H atoms, except the amide NH atoms, have been omitted for clarity. Hydrogen-bonding interactions are shown as dashed lines.

Experimental

Piperidine (245 µl, 2.48 mmol) was dissolved in CH_2Cl_2 (25 ml) in a dry 25 ml flask to which triethylamine (380 µl, 2.73 mmol) was added. The solution was cooled to 273 K and bromoacetyl bromide (216 µl, 2.48 mmol) was added dropwise to the stirred solution. After 15 min, the solution was placed in a separatory funnel and washed with water (20 ml), 5% citric acid (20 ml) and saturated sodium bicarbonate (20 ml). The organic layer was dried over sodium sulfate and filtered. Removal of the solvent *in vacuo* yielded 425 mg of a dark-brown liquid. A 200 mg (0.97 mmol) portion of this liquid was dissolved in *N*,*N*′-dimethylformamide (DMF, 20 ml) and stirred at 273 K. Racemic 1-(pentafluorophenyl)ethylamine (225 mg, 1.07 mmol) was dissolved in DMF (15 ml) and added dropwise to this solution. The solution was stirred for 10 min after the addition was complete, then heated to 343 K for 40 min in an oil bath to afford a mixture of products, presumably including (I). After cooling to room temperature, acetyl chloride (345 µl, 4.85 mmol) and pyridine (118 µl, 1.46 mmol) were added to the crude mixture. The reaction was stirred overnight and the solution was concentrated *in vacuo* to yield a brown oil. The oil was dissolved in CH_2Cl_2 (10 ml). Pyridine (156 µl, 1.94 mmol) was added to the solution, followed by acetyl chloride (345 µl, 4.85 mmol). The solution was stirred for 15 min, followed by removal of the solvent *in vacuo* to yield a gray solid. The solid was redissolved in CH_2Cl_2 (15 ml), placed in a separatory funnel, and washed with 10% citric acid (15 ml) and saturated sodium bicarbonate (15 ml). The organic layer was dried over sodium sulfate, filtered and concentrated *in vacuo* to yield a brown oil. Purification by silica-gel chromatography using ethyl acetate as eluent afforded the desired

product and 123.6 mg of by-products (R_F = 0.6). ^{1}H NMR analysis of the by-products in $CDCl_3$ (300 MHz) indicated the mixture likely consisted of compounds (II) and (III) in an approximate 3:2 ratio. The mixture was dissolved in 1:1 *n*-heptane–chloroform and the solution was allowed to evaporate at room temperature, yielding colorless crystals.

Crystal data

$C_{10}H_8F_5NO$
M_r = 253.17
Triclinic, $P\overline{1}$
a = 7.4129 (5) Å
b = 12.2875 (8) Å
c = 23.5594 (15) Å
α = 77.694 (2)°
β = 82.070 (2)°
γ = 89.936 (2)°
V = 2075.7 (2) Å^3
Z = 8
D_x = 1.620 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.17 mm^{-1}
T = 100 (2) K
Block, colorless
0.49 × 0.38 × 0.26 mm

Data collection

Bruker CCD-1000 area-detector diffractometer
0.30° ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2003)
T_{min} = 0.923, T_{max} = 0.958
30498 measured reflections
8472 independent reflections
6949 reflections with $I > 2\sigma(I)$
R_{int} = 0.024
θ_{max} = 26.4°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.089
S = 1.04
8472 reflections
621 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0417P)^2 + 0.8749P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1*A*—C2*A*	1.2352 (17)	N1*B*—C2*B*	1.3406 (18)
O1*B*—C2*B*	1.2307 (17)	N1*B*—C3*B*	1.4607 (17)
O1*C*—C2*C*	1.2314 (17)	N1*C*—C2*C*	1.3384 (17)
O1*D*—C2*D*	1.2303 (17)	N1*C*—C3*C*	1.4564 (17)
N1*A*—C2*A*	1.3374 (17)	N1*D*—C2*D*	1.3433 (18)
N1*A*—C3*A*	1.4570 (17)	N1*D*—C3*D*	1.4581 (17)
C2*A*—N1*A*—C3*A*	120.90 (11)	C2*C*—N1*C*—C3*C*	121.35 (11)
C2*B*—N1*B*—C3*B*	121.05 (11)	C2*D*—N1*D*—C3*D*	120.96 (11)
C3*A*—N1*A*—C2*A*—O1*A*	−4.2 (2)	C3*C*—N1*C*—C2*C*—O1*C*	0.3 (2)
C3*A*—N1*A*—C2*A*—C1*A*	175.77 (12)	C3*C*—N1*C*—C2*C*—C1*C*	−179.29 (12)
C2*A*—N1*A*—C3*A*—C5*A*	74.23 (15)	C2*C*—N1*C*—C3*C*—C5*C*	81.32 (15)
C2*A*—N1*A*—C3*A*—C4*A*	−163.15 (12)	C2*C*—N1*C*—C3*C*—C4*C*	−156.20 (12)
C3*B*—N1*B*—C2*B*—O1*B*	0.5 (2)	C3*D*—N1*D*—C2*D*—O1*D*	3.1 (2)
C3*B*—N1*B*—C2*B*—C1*B*	−179.40 (12)	C3*D*—N1*D*—C2*D*—C1*D*	−176.07 (12)
C2*B*—N1*B*—C3*B*—C5*B*	87.95 (15)	C2*D*—N1*D*—C3*D*—C5*D*	84.22 (15)
C2*B*—N1*B*—C3*B*—C4*B*	−146.12 (13)	C2*D*—N1*D*—C3*D*—C4*D*	−150.02 (12)

All H atoms were placed in idealized locations and refined as riding, with C—H (methyl groups) = 0.98 Å, C3—H = 1.00 Å and N—H = 0.88 Å, and with U_{iso}(H) = 1.2 (for N1 and C3) or 1.5 (for methyl groups) times U_{eq}(parent).

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···O1*D*^{i}	0.88	2.02	2.8443 (15)	156
N1*B*—H1*AA*···O1*A*	0.88	2.03	2.8855 (15)	165
N1*C*—H1*BA*···O1*B*^{ii}	0.88	1.96	2.8380 (15)	172
N1*D*—H1*CA*···O1*C*	0.88	2.00	2.8569 (15)	164

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

Data collection: *SMART* (Bruker, 2003); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2003); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; 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: HJ3006). Services for accessing these data are described at the back of the journal.

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