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5-Benzoylamino-3-bromo-4-(4-methoxyphenyl)-4,5-dihydroisoxazole-5-carboxylic acid

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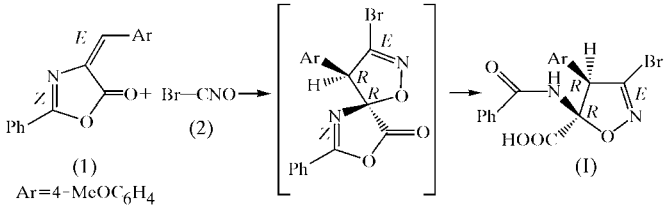
The title compound, $C_{18}H_{15}BrN_2O_5$, a promising N-protected α-amino acid, was synthesized directly from an unusual bromo dipole and a 4-(arylmethylene)oxazolone. The crystal packing of the title compound is a racemic mixture. Peculiar graph-set motifs driven by the most important hydrogen bonds are described.

Comment

As part of a search for biologically active heterocyclic compounds, the α-amino acid (I) was prepared from bromonitrile oxide, (2), and (*Z*)-4-arylmethylene-2-phenyl-1,3-oxazol-5(4*H*)-one, (1) (Foti *et al.*, 2004). The reaction appeared to proceed through complete substrate-controlled diastereoselectivity and the unexpected amino acid, (I), was isolated after the opening of the fragile oxazolone ring.



Compound (I) is an isoxazoline substituted with (i) a Br atom, (ii) a *para*-methoxyphenyl group, (iii) a benzoylamine group and (iv) a carboxylic acid group. The molecule in the asymmetric unit contains two chiral C atoms, C2 and C3, whose configurations are *S* and *R* (Fig. 1). Since the compound crystallizes in the centrosymmetric space group $P2_1/c$, it is a racemic mixture in the solid state. Despite the sp^3 hybridization of these C atoms, the isoxazoline ring appears planar [the maximum deviation from the plane is 0.108 (5) Å for atom C2] because of the extended π conjugation over the other sp^2-hybridized C atom and the heteroatoms (see the geometric parameters for atoms O3 and N2 in Table 1). The amide linkage is found in the usual *trans* conformation [C2—N1—C12—C13 = 179.3 (4)°] and the benzamide moiety, as usual, does not deviate from planarity, allowing extended π conjugation on atoms C12, N1 and O5. The bond distances and angles of the benzamide fragment are in good agreement with the corresponding values reported in related compounds (Buñuel *et al.*, 1996, 1997). Early studies (Domiano *et al.*, 1979) have already noticed a large asymmetry in the methoxy–ring angles for anisole moieties, which has been ascribed to some degree of conjugation between the O atom and the benzene ring. We have found evidence to support this interpretation by analysing the electron density of structures concerning compounds of pharmacological interest and by running theoretical calculations (Bruno *et al.*, 1999, 2001). In this case,

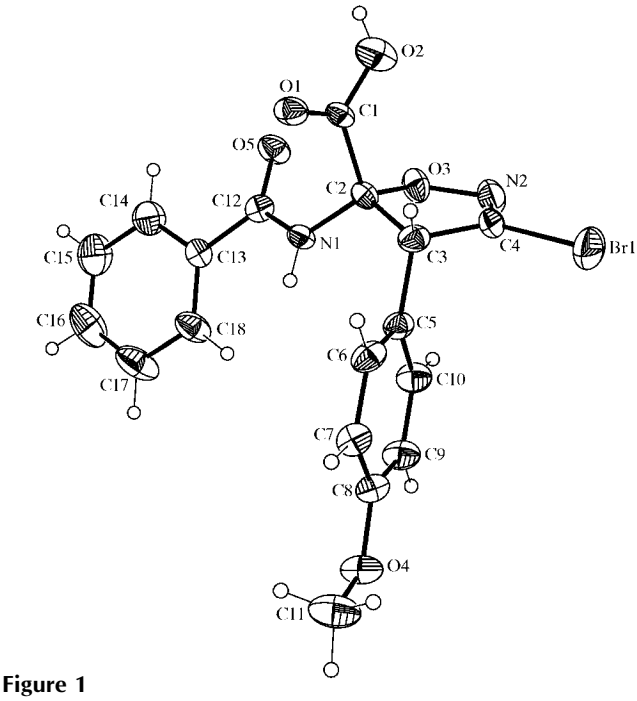


Figure 1
A view of (I), with 30% probability displacement ellipsoids and the atom-numbering scheme.

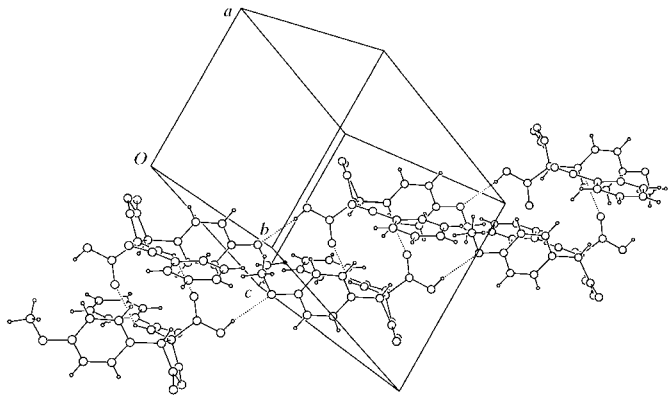


Figure 2
The crystal packing of (I), showing intermolecular interactions as dotted lines.

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the asymmetry is noticeable for the C7—C8—O4 [124.4 (5)°] and C9—C8—O4 [115.7 (4)°] angles, as well as in the planarity of the methoxy group with respect to the benzene ring [C7—C8—O4—C11 = −5.1 (8)°], all of which are determined by conjugation effects. Evident conformational freedom generates disorder for the terminal carboxylic acid and *para*-methoxyphenyl groups, as evidenced by the displacement parameters and structural resolution warnings. The crystal packing is essentially governed by intermolecular hydrogen bonds (Table 2). The most important interaction links two enantiomeric molecules related by an inversion centre. The other noteworthy hydrogen-bonding interaction develops chains along the [101] direction. In summary, the first-level graph-set definition (Bernstein *et al.*, 1995) for this arrangement is $C(10)R_2^2(10)$. The three-dimensional packing takes the form of linear coupled strands running along the [101] axis (Fig. 2).

Experimental

The scheme in the *Comment* illustrates the reaction in tetrahydrofuran leading to the formation of (I), as described by Foti *et al.* (2004). After purification, crystals suitable for X-ray analysis were obtained by slow evaporation from acetone.

Crystal data

$C_{18}H_{15}BrN_2O_5$
M_r = 419.23
Monoclinic, $P2_1/c$
a = 9.9280 (8) Å
b = 19.9509 (17) Å
c = 9.5841 (14) Å
β = 107.875 (9)°
V = 1806.7 (4) Å^3
Z = 4
D_x = 1.541 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 39 reflections
θ = 5.2–13.9°
μ = 2.31 mm^{-1}
T = 298 (2) K
Irregular, colourless
0.50 × 0.38 × 0.30 mm

Data collection

Bruker *P*4 diffractometer
ω scans
Absorption correction: by integration (*XPREPW*; Bruker, 1997)
T_{min} = 0.305, T_{max} = 0.579
3980 measured reflections
3157 independent reflections
1773 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 25.0°
$h = -11 \rightarrow 11$
$k = -1 \rightarrow 23$
$l = -1 \rightarrow 11$
3 standard reflections
every 197 reflections
intensity decay: none

Table 1
Selected geometric parameters (Å, °).

Br1—C4	1.868 (6)	O2—C1	1.338 (6)
N2—C4	1.260 (8)	O3—C2	1.463 (5)
N2—O3	1.421 (6)	O4—C8	1.373 (6)
N1—C2	1.424 (6)	O4—C11	1.422 (7)
O1—C1	1.220 (6)		
C4—N2—O3	107.2 (5)	O4—C8—C7	124.4 (5)
C12—N1—C2	120.7 (4)	O4—C8—C9	115.7 (4)
N2—O3—C2	109.5 (4)	C7—C8—C9	119.9 (5)
C8—O4—C11	116.7 (4)		
C4—N2—O3—C2	9.3 (6)	O5—C12—C13—C14	−18.6 (7)
O3—N2—C4—C3	2.4 (7)	N1—C12—C13—C14	162.3 (5)
C2—C3—C4—N2	−11.9 (6)	O5—C12—C13—C18	158.6 (5)
C11—O4—C8—C7	−5.1 (8)	N1—C12—C13—C18	−20.6 (7)
C11—O4—C8—C9	176.4 (5)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^{i}	0.86	2.31	2.963 (5)	133
O2—H2···O4^{ii}	0.82	2.33	3.139 (6)	170

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.149
S = 1.02
3157 reflections
237 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0481P)^2 + 3.8612P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.65 e Å^{-3}
$\Delta\rho_{min}$ = −0.86 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0040 (7)

H atoms were located in a difference Fourier map, and were then placed in idealized positions and included in the refinement using a riding model.

Data collection: *XSCANS* (Siemens, 1989); cell refinement: *XSCANS*; data reduction: *XPREPW* (Bruker, 1997); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XPW* (Bruker, 1997); software used to prepare material for publication: *PARST*97 (Nardelli, 1995) and *WinGX-PC* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1666). Services for accessing these data are described at the back of the journal.

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