

Ethyl 2-formamido-2-(4-iodobenzyl)-3-(4-iodophenyl)propionate and ethyl 2-(3-bromobenzyl)-3-(3-bromophenyl)-2-formamidopropionate

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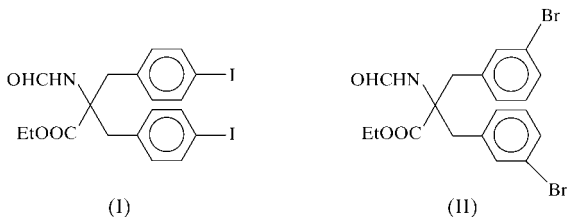
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The title compounds, C₁₉H₁₉I₂NO₃ and C₁₉H₁₉Br₂NO₃, are derivatives of α -aminoisobutyric acid with halogen substituents at the *para* and *meta* positions, respectively. The ethoxycarbonyl and formamide side chains attached to the C α atom of the molecule adopt extended and folded conformations, respectively. The crystal structures are stabilized by N—H...O, C—H...O, C—Br...O and C—I...O interactions.

Comment

Recently, there has been increasing interest in the synthesis of structural variations of α -aminoisobutyric acid (Aib) with the aim of incorporating them into peptides (Karle *et al.*, 1994; Ramesh & Balaram, 1999; Formaggio *et al.*, 2000). Dibenzylglycine (Dbzg) is a special structural variant of Aib (Kotha *et al.*, 2002; Scott *et al.*, 1997). The presence of two benzyl groups at the α position of Dbzg not only gives rigidity to the peptide backbone, but also acts as a useful vehicle for studying π – π interactions (Studer & Seebach, 1995; Damodharan, Shama-ladevi *et al.*, 2002). In this paper, we present the crystal structures of two derivatives of Dbzg with iodine and bromine substituted at the *para* and *meta* position of the benzene rings, namely ethyl 2-formamido-2-(4-iodobenzyl)-3-(4-iodophenyl)propionate, (I), and ethyl 2-(3-bromobenzyl)-3-(3-bromophenyl)-2-formamidopropionate, (II).



Compound (I) crystallizes from acetone–dichloromethane (1:1) and compound (II) crystallizes from *n*-propanol-di-

chloromethane (1:3), both in the $P2_1/n$ space group (Fig. 1). The I and Br atoms are coplanar with their respective benzene rings. The ethoxycarbonyl and formamide side chains adopt extended and folded conformations in both compounds [C1—N1—C19—O19 = 2.8 (8) and 2.1 (7)°, and C16—O17—C17—C18 = –175.8 (7) and –169 (1)° in (I) and (II), respectively].

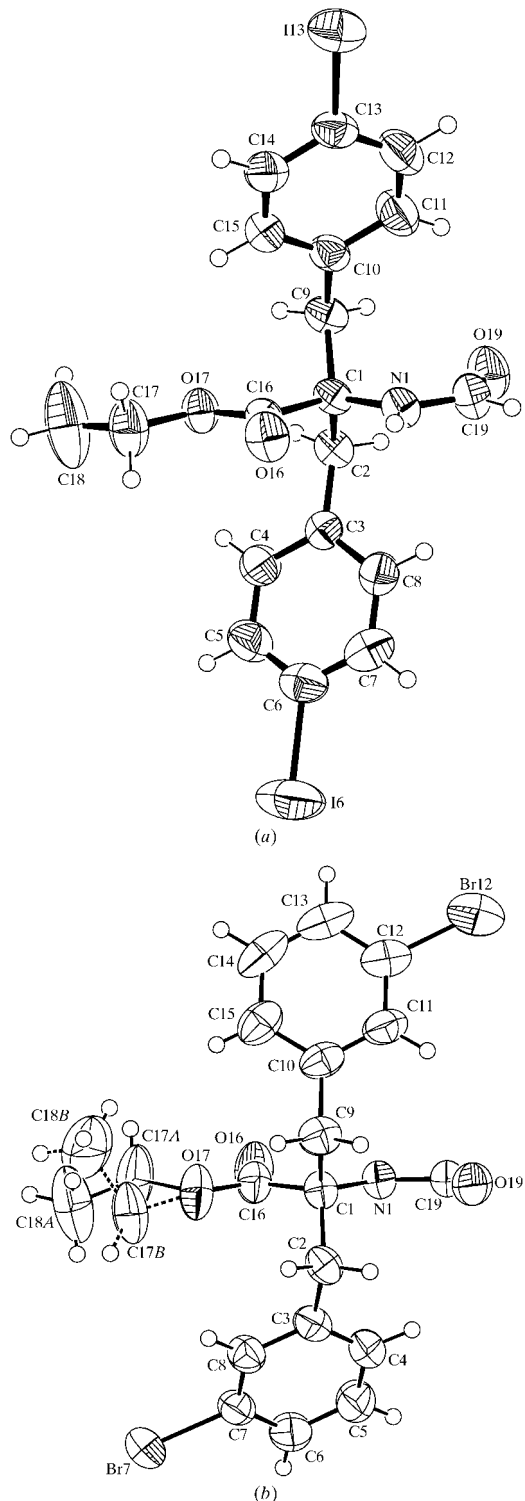


Figure 1
The molecular structures of (a) compound (I) and (b) compound (II), showing 50% probability displacement ellipsoids and the atomic numbering schemes.

The formamide side chain is planar in both compounds. The dihedral angles between the two benzene rings are 68.9 (1) and 62.0 (2)° in (I) and (II), respectively. Terminal atom C18

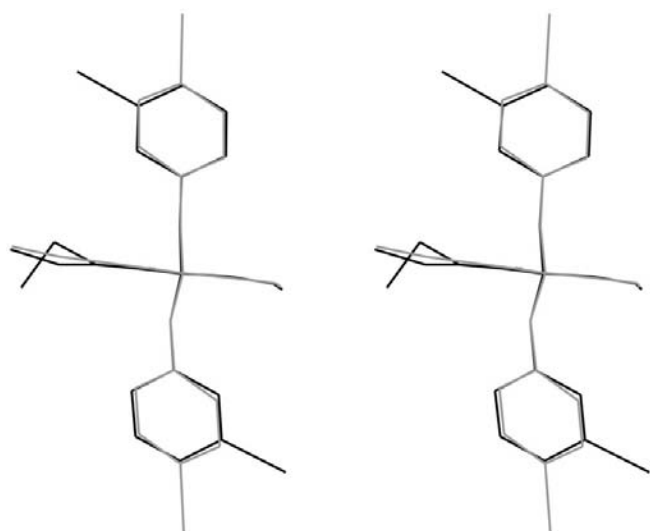


Figure 2
Stereoview of the superposition of compounds (I) (grey) and (II) (black).

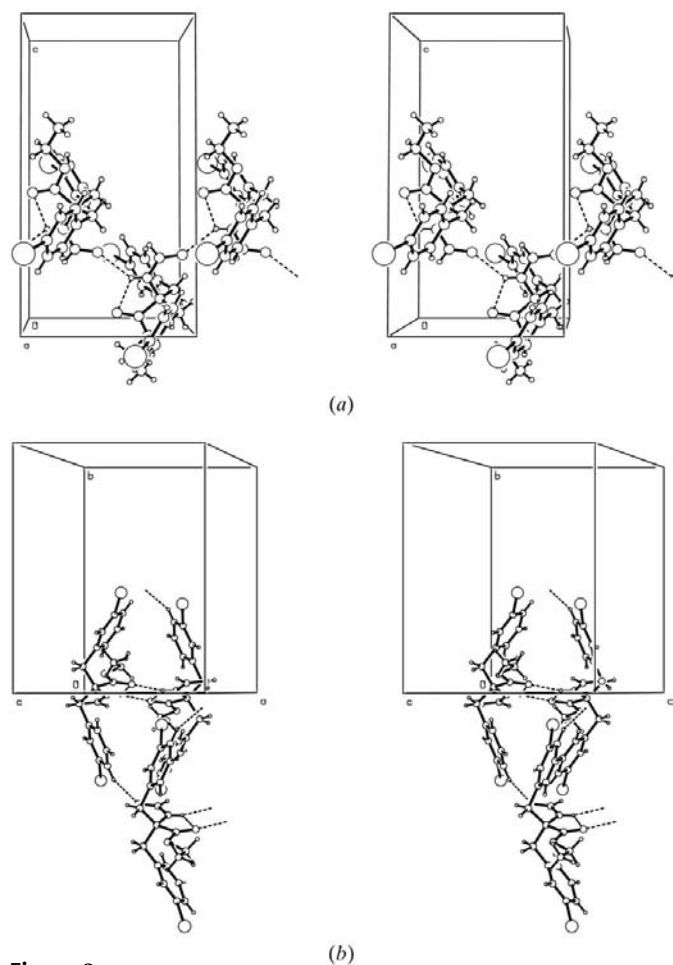


Figure 3
Stereoviews of the packing of (a) molecules of compound (I), showing C—H...O and N—H...O interactions along the *ab* plane, and (b) molecules of compound (II), showing N—H...O interactions along the *bc* plane.

of the ethoxycarbonyl side chain of compound (I) shows high anisotropic displacement parameters and in compound (II) atoms C17 and C18 show disorder. There is no significant variation in the conformations of the two compounds (Fig. 2), except for the angle between the two benzene rings and ethoxycarbonyl side chains.

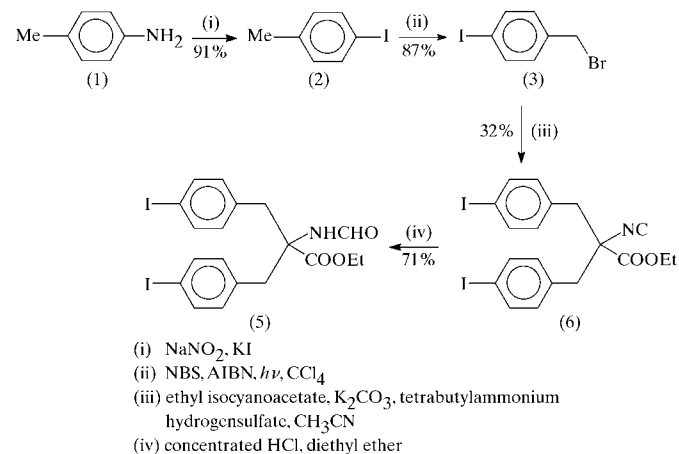
A transannular hydrogen bond (Damodharan, Syed Ibrahim *et al.*, 2002), N1—H...O16, connecting symmetry-related molecules, is present in compound (II). Compound (I) is devoid of this transannular hydrogen bond due to steric clashes of the I atom at the *para* position with its symmetry-related molecule. Atom N1 of the formamide side chain of (I) participates in a three-centred N—H...O interaction with atoms O16 and O19ⁱ (Table 1). In compound (II), the N1—H1...O16 hydrogen bond is bifurcated (Table 2). A C—I...O interaction has also been observed in the packing of compound (I) (Fig. 3a); the I13...O16(−*x*, 1 − *y*, −*z*) distance is 3.333 (4) Å.

The C7—Br7 and C12—Br12 bond lengths are 1.901 (4) and 1.923 (6) Å, respectively, in compound (II), which are longer than the accepted value of 1.89 Å for bromine bonded to a *Csp*² atom. The elongation of the C12—Br12 bond may be due to the electron-withdrawing nature of the Br atom (Dewar & Schmeizing, 1969; Leser & Rabinovich, 1978).

A C—Br...O interaction is observed in the packing of compound (II) (Fig. 3b); the Br7...O19($\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z$) distance is 3.053 (3) Å. Hassel & Roming (1962) have also observed the presence of an attractive interaction between a bonded halogen atom and an O atom, and interpreted it as a charge transfer between an electron-pair donor (O, N or S) and an electron-pair acceptor.

Experimental

Compound (I) was synthesized under phase-transfer conditions (PTC) using ethyl isocyanoacetate as a glycine equivalent (see reaction *Scheme* below) in a four-step sequence starting from *p*-toluidine (Kotha & Brahmachary, 1997, 2000). Thus, diazotization of compound (1) and subsequent iodination of the diazo derivative



with KI gave 4-iodotoluene, (2). Benzylic bromination of (2) with *N*-bromosuccinimide under 2,2'-azobisisobutyronitrile/CCl₄ reflux conditions gave (3). Alkylation of ethyl isocyanoacetate with (3)

under PTC conditions gave the dialkylated product (4). Hydrolysis of the coupling product was achieved by treating (4) in HCl/diethyl ether/H₂O solution at room temperature for a few hours to give the title formamide derivative, (I). A similar procedure was used for the synthesis of compound (II).

Compound (I)

Crystal data

C ₁₉ H ₁₉ I ₂ NO ₃	$D_x = 1.816 \text{ Mg m}^{-3}$
$M_r = 563.15$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 3103 reflections
$a = 13.982(7) \text{ \AA}$	$\theta = 2.3\text{--}26.2^\circ$
$b = 8.922(5) \text{ \AA}$	$\mu = 3.07 \text{ mm}^{-1}$
$c = 16.533(8) \text{ \AA}$	$T = 293(2) \text{ K}$
$\beta = 92.976(8)^\circ$	Prism, colourless
$V = 2059.8(18) \text{ \AA}^3$	$0.76 \times 0.46 \times 0.29 \text{ mm}$
$Z = 4$	

Data collection

Bruker SMART APEX diffractometer	4852 independent reflections
ω scans	4008 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SADABS; Bruker, 1999)	$R_{\text{int}} = 0.036$
$T_{\text{min}} = 0.203$, $T_{\text{max}} = 0.472$	$\theta_{\text{max}} = 28.2^\circ$
32 912 measured reflections	$h = -18 \rightarrow 18$
	$k = -11 \rightarrow 11$
	$l = -21 \rightarrow 21$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0899P)^2 + 2.9260P]$
$R[F^2 > 2\sigma(F^2)] = 0.056$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.160$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.01$	$\Delta\rho_{\text{max}} = 1.47 \text{ e \AA}^{-3}$
4852 reflections	$\Delta\rho_{\text{min}} = -0.58 \text{ e \AA}^{-3}$
226 parameters	
H-atom parameters constrained	

Table 1

Hydrogen-bonding and short-contact geometry (\AA , $^\circ$) for (I).

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
N1—H1 \cdots O19 ⁱ	0.86	2.26	2.975 (5)	141
C9—H9A \cdots O19	0.97	2.53	3.080 (6)	116
C9—H9B \cdots O17	0.97	2.57	2.896 (5)	100
C2—H2B \cdots O19	0.97	2.51	3.133 (6)	122
N1—H1 \cdots O16	0.86	2.23	2.643 (5)	110

Symmetry code: (i) $\frac{1}{2} - x, \frac{1}{2} + y, -\frac{1}{2} - z$.

Compound (II)

Crystal data

C ₁₉ H ₁₉ Br ₂ NO ₃	$D_x = 1.569 \text{ Mg m}^{-3}$
$M_r = 469.17$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 4648 reflections
$a = 11.380(3) \text{ \AA}$	$\theta = 2.1\text{--}29.8^\circ$
$b = 14.867(3) \text{ \AA}$	$\mu = 4.10 \text{ mm}^{-1}$
$c = 12.525(3) \text{ \AA}$	$T = 293(2) \text{ K}$
$\beta = 110.431(4)^\circ$	Irregular, colourless
$V = 1985.8(7) \text{ \AA}^3$	$0.43 \times 0.25 \times 0.18 \text{ mm}$
$Z = 4$	

Data collection

Bruker CCD area-detector diffractometer	4648 independent reflections
φ and ω scans	2163 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SADABS; Bruker, 1999)	$R_{\text{int}} = 0.092$
$T_{\text{min}} = 0.272$, $T_{\text{max}} = 0.526$	$\theta_{\text{max}} = 28.0^\circ$
17 080 measured reflections	$h = -14 \rightarrow 14$
	$k = -19 \rightarrow 19$
	$l = -14 \rightarrow 16$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0772P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.051$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.147$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 0.88$	$\Delta\rho_{\text{max}} = 1.14 \text{ e \AA}^{-3}$
4648 reflections	$\Delta\rho_{\text{min}} = -0.74 \text{ e \AA}^{-3}$
242 parameters	
H-atom parameters constrained	

Table 2

Hydrogen-bonding and short-contact geometry (\AA , $^\circ$) for (II).

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
N1—H1 \cdots O16	0.86	2.20	2.620 (4)	110
C2—H2B \cdots O19	0.97	2.61	3.205 (5)	120
C9—H9A \cdots O19	0.97	2.56	3.095 (6)	115
N1—H1 \cdots O16 ⁱ	0.86	2.18	2.959 (5)	150

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

The H atoms were fixed geometrically at calculated positions (N—H = 0.86 \AA and C—H = 0.93–0.97 \AA). The maximum electron-density peaks are located 0.77 \AA from I6 and 1.09 \AA from Br12 in (I) and (II), respectively.

For both compounds, data collection: SMART (Bruker, 1999); cell refinement: SAINT (Bruker, 1999); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1999); software used to prepare material for publication: SHELXL97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1593). Services for accessing these data are described at the back of the journal.

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