Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å$^2$)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

| | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| C1 | 0.6524 (4) | −0.4681 (7) | 0.2318 (3) | 0.060 (3) |
| S2 | 0.5794 (1) | −0.3438 (2) | 0.1592 (1) | 0.064 (1) |
| C3 | 0.6584 (4) | −0.1493 (7) | 0.1610 (2) | 0.055 (2) |
| C4 | 0.6761 (4) | −0.0487 (6) | 0.2283 (2) | 0.043 (2) |
| C5 | 0.7744 (4) | −0.0530 (7) | 0.2716 (3) | 0.053 (2) |
| C6 | 0.7925 (4) | 0.0201 (7) | 0.3370 (3) | 0.052 (2) |
| C7 | 0.7127 (4) | 0.0931 (6) | 0.3594 (3) | 0.046 (2) |
| C8 | 0.6126 (4) | 0.1019 (6) | 0.3177 (2) | 0.039 (2) |
| C9 | 0.5952 (3) | 0.0333 (6) | 0.2503 (2) | 0.038 (2) |
| C10 | 0.5283 (3) | 0.1805 (6) | 0.3462 (2) | 0.044 (2) |
| S11 | 0.5085 (1) | 0.0654 (2) | 0.4219 (1) | 0.049 (1) |
| C12 | 0.4671 (3) | −0.1552 (6) | 0.3898 (2) | 0.044 (2) |
| C13 | 0.5550 (3) | −0.2727 (6) | 0.3811 (2) | 0.038 (2) |
| C14 | 0.6308 (4) | −0.3319 (7) | 0.4371 (3) | 0.052 (2) |
| C15 | 0.7123 (4) | −0.4343 (7) | 0.4261 (3) | 0.060 (2) |
| C16 | 0.7187 (4) | −0.4761 (6) | 0.3607 (3) | 0.053 (2) |
| C17 | 0.6426 (4) | −0.4186 (6) | 0.3042 (3) | 0.043 (2) |
| C18 | 0.5594 (3) | −0.3207 (6) | 0.3146 (2) | 0.038 (2) |
| C19 | 0.4878 (4) | 0.0446 (7) | 0.2042 (2) | 0.044 (2) |
| O20 | 0.4113 (3) | −0.0128 (5) | 0.2173 (2) | 0.058 (1) |
| O21 | 0.4909 (2) | 0.1316 (4) | 0.1461 (2) | 0.049 (1) |
| C22 | 0.3945 (4) | 0.1717 (8) | 0.0926 (2) | 0.058 (2) |
| C23 | 0.4365 (4) | 0.2628 (8) | 0.0379 (2) | 0.078 (3) |
| C24 | 0.3382 (4) | 0.0036 (8) | 0.0657 (3) | 0.085 (3) |
| C25 | 0.3276 (4) | 0.2938 (8) | 0.1235 (3) | 0.083 (3) |

Table 2. *Selected bond distances* (Å) *and angles* (°)

| | | | |
|---|---|---|---|
| C1—S2 | 1.805 (5) | C19—O20 | 1.196 (7) |
| S2—C3 | 1.815 (5) | C19—O21 | 1.345 (6) |
| C10—S11 | 1.820 (5) | O21—C22 | 1.487 (5) |
| S11—C12 | 1.836 (5) | C22—C23 | 1.513 (8) |
| C1—S2—C3 | 102.5 (2) | C10—S11—C12 | 104.2 (2) |

The title compound was synthesized by reaction of 2,6-bis-(bromomethyl)benzoic acid *tert*-butyl ester and 1,3-bis(mercaptomethyl)benzene in benzene–ethanol (1:1) with sodium hydroxide as base under high-dilution conditions (Vögtle, Grütze, Nätscher, Wieder, Weber & Grün, 1975). Crystals were grown by recrystallization from acetone and were glued on a glass fibre.

The structure was solved by direct methods (Sheldrick, 1986) and refinement was by full-matrix least-squares techniques (Sheldrick, 1976). H atoms were included at calculated positions (C—H = 1.08 Å), riding on the carbon skeleton in the final stages of refinement with a common isotropic displacement parameter for the CH, $CH_2$ and $CH_3$ groups. Distances and angles were calculated by *PARST* (Nardelli, 1983).

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and bond lengths and angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71309 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: SH1046]

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# Structure of (*Z*)-L-Pro-D-(α*Me*)Phe-OH

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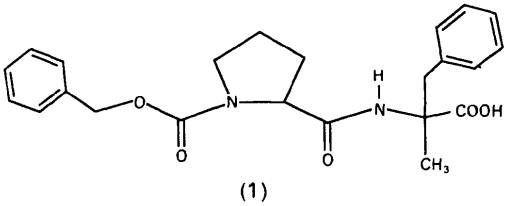
## Abstract

In this N-protected heterochiral dipeptide ($N^{\alpha}$-benzyloxycarbonyl-L-prolyl-$C^{\alpha}$-methyl-D-phenylalanine), the tertiary urethane moiety is *cis*. In addition, the L-Pro residue is semi-extended while the D-(α*Me*)Phe residue is fully extended.


## Comment

In connection with our current investigation into analogues at position 3 of morphiceptin, a pentapeptide amide with extreme selectivity for the μ-opiate receptor, the X-ray diffraction analysis of the title compound ($N^{\alpha}$-benzyloxycarbonyl-L-prolyl-$C^{\alpha}$-methyl-D-phenylalanine) (1) was carried out to determine the structural preference of this conformationally constrained heterochiral dipeptide sequence. Details of the synthetic work will be published elsewhere (Formaggio, Crisma, Toniolo & Kamphuis, 1993).




(1)

The L-Pro residue of this N-protected dipeptide is semi-extended with backbone torsion angles $\varphi_1$ and $\psi_1$ (IUPAC–IUB Commission on Biochemical Nomenclature, 1970) of −74.8 (4) and 146.7 (3)°, respectively. The D-($\alpha$Me)Phe residue adopts the fully extended intramolecularly hydrogen-bonded $C_5$ conformation [$\varphi_2$, $\psi_T$ = −179.5 (3), 178.2 (3)°] (Toniolo & Benedetti, 1991). The intramolecular N2···O4 separation is 2.630 (4) Å. The N2—C14—C16($\tau$) bond angle is 105.9 (3)°. The $\chi_2^1$ side-chain torsion angle (Benedetti, Morelli, Nemethy & Scheraga, 1983) for the D-($\alpha$Me)Phe residue is *gauche*$^-$ [−52.3 (4)°], while the $\chi_2^{2,1}$ and $\chi_2^{2,2}$ torsion angles are −88.7 (5) and 90.5 (5)°, respectively. The —CO—N< (*Z*)-urethane moiety is *cis* [$\omega_o$ = −7.5 (5)°], a rather common observation for *tertiary* —CO—N< groups (Benedetti, Pedone, Toniolo, Dudek, Nemethy & Scheraga, 1983). The peptide group is *trans* planar [$\omega_1$ = −178.9 (3)°] (Benedetti, 1982).

In the crystals, the molecules pack by forming chains of intermolecular hydrogen bonds of the (carboxylic) O—H···O=C (peptide) and (peptide) N—H···O=C (urethane) types along the *y* direction. The O5···O3($-x, \frac{1}{2}+y, -\frac{3}{2}-z$) distance [2.530 (3) Å] is rather short (Mitra & Ramakrishnan, 1977), while the N2···O2($-x, \frac{1}{2}+y, -\frac{1}{2}-z$) distance [3.022 (4) Å] is normal (Görbitz, 1989). Interestingly, an intermolecular hydrogen bond N2—H···O2 is observed rather than formation of the intramolecular interaction typical of the $C_7(\gamma)$-turn conformation (Nemethy & Printz, 1972).

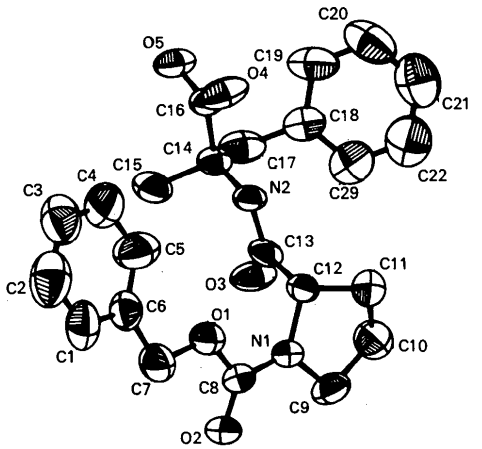



Fig. 1. View of the *Z*-L-Pro-D-($\alpha$Me)Phe-OH molecule showing the labelling of the non-H atoms. Thermal ellipsoids are shown at 50% probability levels.

## Experimental

*Crystal data*

$C_{23}H_{26}N_2O_5$
$M_r$ = 410.48
Orthorhombic
$P2_12_12_1$
$a$ = 20.841 (2) Å
$b$ = 12.947 (2) Å
$c$ = 8.168 (1) Å
$V$ = 2204.0 (5) Å$^3$
$Z$ = 4
$D_x$ = 1.24 Mg m$^{-3}$
Mo $K\alpha$ radiation
$\lambda$ = 0.7107 Å
Cell parameters from 25 reflections
$\theta$ = 7–12°
$\mu$ = 0.082 mm$^{-1}$
$T$ = 293 K
Plate
0.8 × 0.7 × 0.2 mm
Colourless

*Data collection*

Philips PW1100 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
3046 measured reflections
3020 independent reflections
1512 observed reflections [$F \geq 7\sigma(F)$]
$R_{int}$ = 0
$\theta_{max}$ = 28°
$h$ = 0 → 27
$k$ = 0 → 17
$l$ = 0 → 10
3 standard reflections
frequency: 180 min
intensity variation: 10%

*Refinement*

Refinement on $F$
Final $R$ = 0.046
$wR$ = 0.053
$S$ = 1.190
1512 reflections
343 parameters
$w = 1/[\sigma^2(F) + 0.0017F^2]$
$(\Delta/\sigma)_{max}$ = 0.073
$\Delta\rho_{max}$ = 0.14 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.17 e Å$^{-3}$
Atomic scattering factors from Cromer (1974) and Cromer & Waber (1974)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å$^2$)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

| | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| O1 | −0.0708 (1) | −0.7649 (2) | −0.2507 (4) | 0.073 (1) |
| O2 | −0.0331 (1) | −0.9246 (2) | −0.1885 (4) | 0.0726 (9) |
| O3 | 0.0478 (2) | −0.7584 (2) | −0.5754 (3) | 0.085 (1) |
| O4 | −0.0386 (2) | −0.4164 (2) | −0.6421 (4) | 0.083 (1) |
| O5 | −0.0422 (2) | −0.4533 (2) | −0.9080 (3) | 0.073 (1) |
| N1 | 0.0342 (1) | −0.7910 (2) | −0.2444 (4) | 0.062 (1) |
| N2 | 0.0101 (1) | −0.5958 (2) | −0.5561 (3) | 0.051 (1) |
| C1 | −0.2445 (2) | −0.7221 (4) | −0.2043 (8) | 0.094 (2) |
| C2 | −0.2898 (2) | −0.6510 (6) | −0.247 (1) | 0.113 (3) |
| C3 | −0.2735 (3) | −0.5697 (5) | −0.344 (1) | 0.115 (3) |
| C4 | −0.2103 (3) | −0.5584 (4) | −0.401 (1) | 0.122 (3) |
| C5 | −0.1643 (2) | −0.6314 (4) | −0.3558 (8) | 0.099 (2) |
| C6 | −0.1816 (2) | −0.7143 (3) | −0.2582 (6) | 0.074 (2) |
| C7 | −0.1350 (2) | −0.7973 (4) | −0.2119 (7) | 0.081 (2) |
| C8 | −0.0233 (2) | −0.8345 (3) | −0.2253 (5) | 0.061 (1) |
| C9 | 0.0941 (2) | −0.8512 (3) | −0.2215 (6) | 0.067 (1) |
| C10 | 0.1460 (2) | −0.7763 (3) | −0.2819 (7) | 0.084 (2) |
| C11 | 0.1173 (2) | −0.6704 (3) | −0.2669 (6) | 0.064 (1) |
| C12 | 0.0452 (2) | −0.6856 (3) | −0.3057 (4) | 0.054 (1) |
| C13 | 0.0341 (2) | −0.6821 (3) | −0.4903 (4) | 0.054 (1) |
| C14 | −0.0035 (2) | −0.5849 (2) | −0.7313 (5) | 0.057 (1) |
| C15 | −0.0559 (3) | −0.6608 (3) | −0.7866 (6) | 0.086 (2) |
| C16 | −0.0295 (2) | −0.4751 (2) | −0.7537 (5) | 0.055 (1) |
| C17 | 0.0568 (2) | −0.5980 (3) | −0.8407 (5) | 0.070 (1) |
| C18 | 0.1127 (2) | −0.5313 (3) | −0.7937 (5) | 0.065 (1) |
| C19 | 0.1196 (2) | −0.4319 (4) | −0.8574 (7) | 0.094 (2) |
| C20 | 0.1714 (3) | −0.3699 (4) | −0.809 (1) | 0.120 (3) |
| C21 | 0.2163 (3) | −0.4050 (6) | −0.699 (1) | 0.120 (3) |
| C22 | 0.2093 (3) | −0.5021 (6) | −0.6354 (8) | 0.118 (3) |
| C23 | 0.1586 (3) | −0.5646 (4) | −0.6848 (6) | 0.091 (2) |

Table 2. *Geometric parameters* (Å, °)

| | | | |
|---|---|---|---|
| O1—C7 | 1.438 (5) | N2—C13 | 1.338 (4) |
| O1—C8 | 1.354 (4) | N2—C14 | 1.465 (5) |
| O2—C8 | 1.222 (4) | C9—C10 | 1.534 (6) |
| O3—C13 | 1.241 (4) | C10—C11 | 1.501 (6) |
| O4—C16 | 1.202 (5) | C11—C12 | 1.548 (5) |
| O5—C16 | 1.318 (5) | C12—C13 | 1.526 (5) |
| N1—C8 | 1.332 (4) | C14—C15 | 1.537 (6) |
| N1—C9 | 1.484 (5) | C14—C16 | 1.534 (5) |
| N1—C12 | 1.472 (4) | C14—C17 | 1.551 (6) |
| C7—O1—C8 | 117.0 (3) | O3—C13—C12 | 119.7 (3) |
| C9—N1—C12 | 113.5 (3) | O3—C13—N2 | 121.8 (3) |
| C8—N1—C12 | 124.9 (3) | N2—C14—C17 | 113.3 (3) |
| C8—N1—C9 | 121.3 (3) | N2—C14—C16 | 105.9 (3) |
| C13—N2—C14 | 123.0 (3) | N2—C14—C15 | 111.3 (3) |
| O1—C7—C6 | 109.9 (3) | C16—C14—C17 | 108.6 (3) |
| O2—C8—N1 | 125.7 (3) | C15—C14—C17 | 109.7 (3) |
| O1—C8—N1 | 110.9 (3) | C15—C14—C16 | 107.8 (3) |
| O1—C8—O2 | 123.4 (3) | O5—C16—C14 | 112.5 (3) |
| N1—C9—C10 | 102.8 (3) | O4—C16—C14 | 123.5 (4) |
| N1—C12—C13 | 109.9 (3) | O4—C16—O5 | 124.0 (3) |
| N2—C13—C12 | 118.6 (3) | C14—C17—C18 | 114.7 (3) |

Program used to solve structure: *SHELXS86* (Sheldrick, 1986). The structure was refined by blocked full-matrix least squares with anisotropic thermal parameters for all non-H atoms. H atoms were either located on a $\Delta F$ map or calculated. The H atoms attached to C1, C2, C3, C4, C5 and C15 were not refined; all other H atoms were refined isotropically. Program used to refine structure: *SHELX76* (Sheldrick, 1976).

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71302 (19 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: CD1011]

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# Structure of Bis(2-amino-5-benzoylphenyl) Diselenide

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## Abstract

The title compound, 3,3′-diselenobis(4-aminobenzophenone), is one of a series of antioxidant drugs, which has glutathione peroxidase activity. This diselenide can be generated *in vivo* by administration of the corresponding benzoselenazolinone as a pro-drug. It is important to correlate the structure with the pharmacological parameters. In an initial approach the structure of this compound was determined by X-ray analysis; this, in turn, dictates the structure of the corresponding benzoyl benzoselenazolinone.

## Comment

Recently, simple seleno-organic compounds were shown to mimic *in vitro* the enzymic activity of glutathione peroxidase, an important system of cell defence against oxidative stress (Parnham & Graf, 1987; Günzler, Steffens & Grossman, 1982). Such molecules are able to convert hydroperoxides into alcohols with their selenium-containing active centre. The catalytic process involves a selenolate anion, as the active form, reducing hydroperoxides (Günzler, Steffens & Grossman, 1982). An isoselenazolin-3-one ring or a diselenide entity are then generated as reaction products (Reich & Jasperse, 1987; Parnham & Kindt, 1984; Chan, Cotelle, Cotelle, Bernier & Hénichart, 1991). Finally the active form is restored by a glutathione nucleophilic attack.

The development of synthetic compounds with glutathione peroxidase activity found its basis in the aforementioned catalytic redox cycle. The more promising molecules were 2-phenyl-1,2-benzoselenazol-3(2*H*)-one or ebselen (1), a heterocyclic