

prévu par le calcul conformationnel pour les molécules β -adrénergiques (Léger, 1979). Cette différence est due au remplacement d'un atome d'oxygène divalent dans le propranolol par un atome d'azote trivalent dans l'azapropranolol. Il en résulte que la distance de l'azote N(17) au plan moyen des cycles aromatiques est beaucoup plus longue dans l'azapropranolol (3,1 Å) que dans le propranolol (1,2 Å). Cette différence pourrait expliquer, du moins en partie, l'absence de propriétés β -bloquante de l'azapropranolol puisque cette molécule ne correspond pas au modèle des drogues β -adrénoLytiques défini par Léger, Gadret & Carpy (1979).

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N-Glutaryl-L-phenylalanine *p*-Nitroanilide

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Abstract. $C_{20}H_{21}N_3O_6$, a chymotrypsin substrate, $M_r = 399.4$, crystallizes in the orthorhombic space group $P2_12_12_1$, $a = 22.638$ (4), $b = 7.635$ (1), $c = 11.356$ (2) Å, $Z = 4$. $D_o = 1.352$, $D_c = 1.341$ Mg m $^{-3}$. The structure was solved by *MULTAN* and refined to an R of 0.053 for 1258 reflections. The crystal structure is stabilized by a three-dimensional network of N–H \cdots O and O–H \cdots O hydrogen bonds. The molecule exists in the extended conformation.

Introduction. *N*-Glutaryl-L-phenylalanine *p*-nitroanilide (GPNA), a chymotrypsin substrate and a molecule containing two aromatic groups, has been studied as part of the project on structures of molecules of biological interest. The molecular conformation of this molecule may be of use in comparative and theoretical studies of peptide and amino-acid-derivative conformations. The structure of GPNA is compared with structures of other chymotrypsin substrates like *N*-acetyl-L-tyrosine *p*-nitroanilide (ATNA) (Michel & Durant, 1976) and *N*-acetyl-L-tyrosine ethyl ester (ATEE) (Pieret, Durant, Germain & Koch, 1972).

The compound crystallizes from methanol as thin

needles along the shortest axis. Preliminary cell dimensions were established by rotation and Weissenberg photographs and more accurate values by least-squares refinement from Bragg angles measured at $\pm 2\theta$ ranging from 20 to 120°, on a Picker four-circle diffractometer. The density was measured by flotation in a benzene–bromoform mixture. Intensity data were collected using Fe-filtered Co $K\alpha$ ($\lambda = 1.7903$ Å) radiation and a crystal of 0.3 × 0.4 × 0.4 mm, $\mu = 13.203$ cm $^{-1}$, mounted with its b axis along the ϕ axis of the diffractometer. Reflections with $2\theta \leq 130^\circ$ were scanned in the θ – 2θ mode with a scan speed of 2° min $^{-1}$. Periodic monitoring of a standard reflection did not show any drift. 1258 independent non-zero reflections were measured and corrected for Lorentz and polarization effects.

The structure was solved with *MULTAN* (Main, Woolfson & Germain, 1972). The initial R index for all non-hydrogen atoms was 0.294. The positional and isotropic thermal parameters were refined by least squares. At the end of isotropic refinement, hydrogen atoms were located from a difference synthesis. The successive refinement of positional and anisotropic thermal parameters by the block-diagonal least-squares method (Shiono, 1968) gave an R of 0.084 for 1258

* Contribution No. 583.

Table 1. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters (\AA^2) of non-hydrogen atoms, with *e.s.d.*'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} *
O(1)	-1888 (3)	6533 (10)	5982 (5)	8.09 (4)
O(2)	-1242 (3)	4868 (10)	5149 (5)	9.18 (4)
N(3)	-1435 (3)	5682 (10)	5982 (6)	6.11 (4)
C(4)	-1064 (3)	5722 (10)	7066 (5)	4.04 (4)
C(5)	-0554 (3)	4754 (10)	7069 (5)	4.46 (4)
C(6)	-0211 (3)	4731 (10)	8081 (5)	4.31 (3)
C(7)	-0381 (2)	5670 (9)	9059 (5)	3.41 (3)
C(8)	-0899 (3)	6678 (10)	9018 (6)	4.43 (4)
C(9)	-1246 (3)	6692 (11)	8018 (6)	5.04 (4)
N(10)	-0086 (2)	5636 (7)	10141 (4)	3.46 (2)
C(11)	0473 (2)	5019 (9)	10320 (5)	3.38 (3)
O(12)	0797 (2)	4558 (7)	9537 (3)	4.44 (2)
C(13)	0663 (2)	5015 (9)	11619 (5)	3.18 (3)
N(14)	1168 (2)	3874 (6)	11736 (4)	3.01 (2)
C(15)	1147 (3)	2409 (9)	12368 (5)	3.45 (3)
O(16)	0704 (2)	1923 (7)	12866 (4)	5.30 (3)
C(17)	1713 (3)	1341 (8)	12404 (6)	4.00 (3)
C(18)	2282 (3)	2333 (9)	12785 (5)	3.77 (3)
C(19)	2259 (3)	2702 (9)	14088 (5)	3.85 (3)
C(20)	2790 (3)	3695 (10)	14581 (6)	4.21 (3)
O(21)	3184 (2)	4088 (9)	13761 (4)	6.64 (3)
O(22)	2851 (2)	4079 (8)	15594 (4)	5.24 (3)
C(23)	0821 (3)	6888 (9)	12033 (6)	3.72 (3)
C(24)	0999 (3)	6826 (9)	13337 (5)	3.48 (3)
C(25)	1584 (3)	7090 (9)	13667 (6)	4.14 (4)
C(26)	1748 (3)	7041 (10)	14837 (6)	4.82 (4)
C(27)	1336 (4)	6672 (11)	15704 (6)	5.55 (4)
C(28)	0752 (4)	6363 (11)	15391 (6)	5.65 (4)
C(29)	0582 (3)	6454 (10)	14207 (6)	4.52 (4)

$$* B_{eq} = \frac{1}{3} \times [b_{11}a^2 + b_{22}b^2 + b_{33}c^2] \text{ (Hamilton, 1959).}$$

reflections. The final full-matrix refinement for all non-hydrogen atoms with anisotropic temperature factors, overall scale factor and unit weights was carried out using the program *LALS* (Gantzel, Sparks & Trueblood, 1961). At the end of full-matrix refinement, the reliability index was 0.053.* The hydrogen atoms were included in the structure-factor calculations along with the isotropic temperature factors of the atoms to which they are bonded. Fractional atomic coordinates of the non-hydrogen atoms and their equivalent isotropic thermal parameters are listed in Table 1. Atomic scattering factors are from *International Tables for X-ray Crystallography* (1968).

Discussion. The bond lengths and angles of the GPNA molecule are shown in Fig. 1. The bond lengths and angles of the nitro group and the phenyl group conform to standard values. The molecular packing of the molecules projected down the *b* axis is shown in Fig. 2.

* Lists of structure factors, anisotropic thermal parameters, hydrogen-atom coordinates and least-squares-planes' information have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36817 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

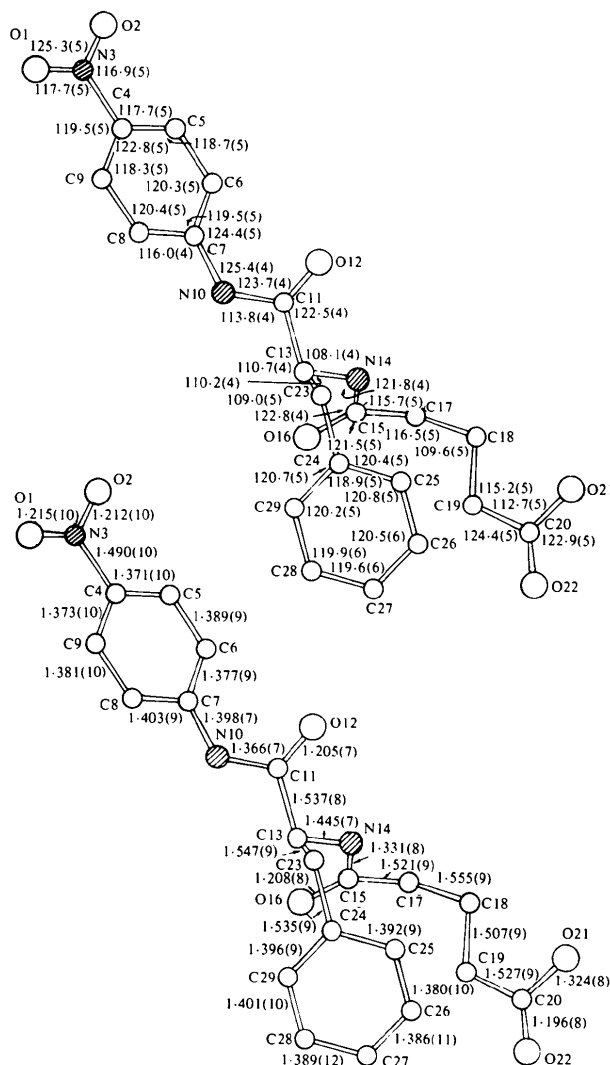


Fig. 1. Bond lengths (\AA) and angles ($^\circ$) of GPNA.

The molecules related by the screw axis in the *b* direction are connected by N(10)—H...O(16) hydrogen bonds. These hydrogen-bonded pairs are held together by van der Waals forces. However, a short intermolecular distance of 3.287 (9) \AA between C(17) and O(2) suggests a C—H...O type hydrogen bond (Sutor, 1962) between these pairs. C(17)—H(17,2)...O(2) and H(17,2)—C(17)...O(2) angles are 137.0 (4) $^\circ$ and 30.0 (4) $^\circ$ respectively. The O(2)...H(17,2) distance is 2.41 (1) \AA . Although the rarity of C—H...O hydrogen bonds is often emphasized, situations very similar to the one we have indicated here have been reported; such C—H...O interactions are listed in Table 2.

The carboxyl group is not ionized and both the phenyl rings are planar within experimental error. The least-squares plane through atoms C(13), N(14),

Table 2. Hydrogen-bonding scheme

D—H...A	D...A (Å)	H...A (Å)	D—H...A (°)	H—D...A (°)
O(21 ^b)—H(21)...O(12)	2.68 (1)	1.70 (1)	167.7 (3)	7.8 (2)
N(10 ^b)—H(10)...O(16 ⁱⁱⁱ)	2.84 (1)	1.85 (1)	154.9 (4)	16.0 (2)
N(14 ^{iv})—H(14)...O(22 ^v)	3.01 (1)	2.16 (1)	155.9 (3)	17.1 (2)

Symmetry operations: (i) $\frac{1}{2} - x, -y, z - \frac{1}{2}$; (ii) $1 - x, y, z - 1$; (iii) $1 - x, \frac{1}{2} + y, \frac{3}{2} - z$; (iv) $x, y, z - 1$; (v) $\frac{1}{2} - x, -y, z - \frac{3}{2}$.

C—H...O interactions

	D...A (Å)	H...A (Å)	D—H...A (°)	Reference
3-Pyridinesulphonic acid	3.262	2.270	159.4	Chandrasekhar (1977)
Glycyl-DL-phenylalanine	3.325	2.40	159.0	Marsh, Ramakumar & Venkatesan (1976)
	3.265	2.39	152.0	
Aqua(glycylglycinato)(9-methyladenine)-copper(II) tetrahydrate	3.194	2.28	156.0	Kistenmacher, Marzilli & Szalda (1976)
<i>N</i> -Glutaryl-L-phenylalanine <i>p</i> -nitroanilide (GPNA)	3.287 (9)	2.41 (1)	137.0 (4)	Present study

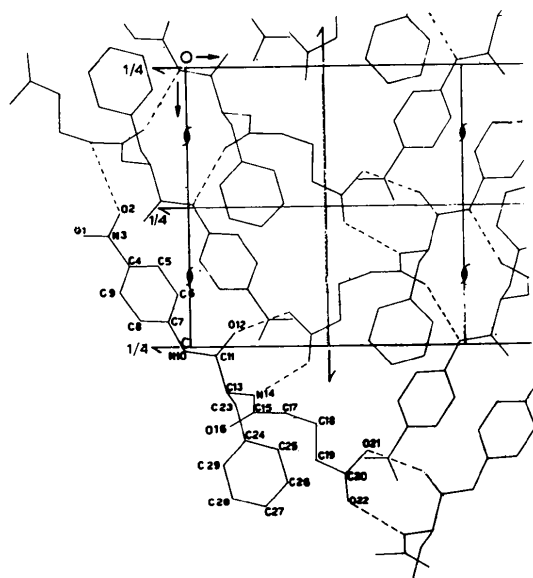


Fig. 2. Packing diagram of GPNA molecule (projection down the *b* axis).

C(15), O(16) and C(17) shows that these atoms lie in a plane with a maximum deviation 0.008 (6) Å. The nitro group makes an angle of 2.8 (1)° with the benzene ring. The two benzene rings make an angle of 129.7 (3)° and the plane containing atoms C(13), N(14), C(15), O(16) and C(17) makes angles of 105.4 (3)° with the nitrophenyl group and 59.0 (1)° with the phenylalanine group. The molecule is stabilized by intermolecular hydrogen bonds of the type N—H...O and O—H...O, which are listed in Table 2.

The torsional angles about the various bonds are listed in Table 3 and the corresponding values for ATNA and ATEE are also listed for comparison. The conformational angles, χ_1 [N(14)—C^α(13)—C^β(23)—C^γ(24)], χ_{21} [C^α(13)—C^β(23)—C^γ(24)—C^δ(25)] and χ_{22} [C^α(13)—C^β(23)—C^γ(24)—C^δ(29)], for the side

Table 3. Torsion angles (°), compared with corresponding angles of ATNA and ATEE

	<i>N</i> -Glutaryl-L-phenylalanine <i>p</i> -nitroanilide (GPNA)	<i>N</i> -Acetyl-L-tyrosine <i>p</i> -nitroanilide (ATNA)	<i>N</i> -acetyl-L-tyrosine ethyl ester (ATEE)
χ_1 [N(14)—C(13)—C(23)—C(24)]	-61.2 (6)	-69.3	-62.9
χ_{21} [C(13)—C(23)—C(24)—C(25)]	109.5 (7)	107.3	117.5
χ_{22} [C(13)—C(23)—C(24)—C(29)]	-68.6 (7)	74.4	64.0
C(8)—C(7)—N(10)—C(11)	-167.3 (6)	144.6	-
ψ_1 [N(14)—C(13)—C(11)—O(12)]	-18.9 (8)	-80.5	-16.4
C(11)—C(13)—N(14)—C(15)	-115.4 (6)	-116.5	-75.2
ψ_2 [N(14)—C(13)—C(11)—N(10)]	162.8 (5)	100.2	164.4
O(16)—C(15)—N(14)—C(13)	1.3 (9)	-6.7	-3.2
C(13)—C(11)—N(10)—C(7)	-175.4 (5)	-170.4	180.0
C(15)—N(14)—C(13)—C(11)	-115.4 (6)	-116.5	-75.2
C(23)—C(13)—C(11)—N(10)	-76.4 (6)	-	-
C(17)—C(15)—N(14)—C(13)	179.7 (5)	-	-
C(15)—C(17)—C(18)—C(19)	72.6 (7)	-	-
C(17)—C(18)—C(19)—C(20)	-179.3 (5)	-	-
C(18)—C(19)—C(20)—O(21)	0.8 (8)	-	-
C(18)—C(19)—C(20)—O(22)	-179.0 (6)	-	-

chain of phenylalanine are -61.2 (6), 109.5 (7) and -68.6 (7)° respectively. C(24) of the side chain is in position III which has also been observed in *N*-(haloacetyl)-L-phenylalanyl-L-phenylalanine ethyl ester (Wei, Doherty & Einstein, 1972) and *D*-phenylalanyl-L-(*O*-methoxyphenylalanine) hydrobromide (Pattabhi & Venkatesan, 1970). The phenyl ring makes an angle of 69.2 (3)° with the C^α(13), C^β(23), C^γ(24) plane. The notation and convention followed is that of Edsall, Flory, Kendrew, Liquori, Nemethy, Ramachandran & Scheraga (1966). If the group involving atoms C(7), N(10), C(11), O(12), C(13), N(14), C(15), C(17) is compared with a peptide group, the torsion angles corresponding to ψ_1 and ψ_2 are -18.9 (8) and 162.8 (5)° for the nitrophenyl end. The atoms C(13), N(14), C(15), O(16) and C(17) lie in a plane and the torsion angle ω [C(13)—N(14)—C(15)—C(17)] is 179.7 (5)°. The above plane is flat and is in the *trans* configuration. The bond lengths and angles in this region agree well with peptide dimensions (Marsh & Donohue, 1967).

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7-Amino-2,4-dimethyl-2*H*,4*H*-1,2,3-triazolo[4,5-*c*] [1,2,6]thiadiazine 5,5-Dioxide

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Abstract. C₇H₈N₆O₂S, *M*_r = 216.22, triclinic, *P*1̄, *Z* = 2, *a* = 7.430 (1), *b* = 8.639 (1), *c* = 7.357 (1) Å, α = 105.24 (1), β = 103.12 (1), γ = 76.55 (1)°, *U* = 436.2 (1) Å³, *D*_c = 1.65 Mg m⁻³, μ(Mo *K*α) = 0.340 mm⁻¹. The structure was refined to *R* = 0.046 for 1402 observed reflexions. The thiadiazine ring was found in the expected envelope conformation. A considerable electron delocalization is detected in the molecular rings. The crystal packing is mainly due to N–H···O and N–H···N hydrogen bonds.

Introduction. This compound has been prepared by Drs Goya, Ochoa and Stud (Inst. Química Médica, CSIC, Madrid) as a part of a research project on heterocyclic compounds containing the thiadiazine group, aimed at obtaining substances with biological activity. The crystal structures of other closely related heterocycles have been reported recently (Foces-Foces, Cano & García-Blanco, 1975*a,b*; Foces-Foces, Cano, García-Blanco & Rodríguez, 1975; Smith-Verdier, Florencio, García-Blanco & Rodríguez, 1977).

A colourless single crystal of dimensions 0.08 × 0.09 × 0.13 mm was used to collect the intensities of 2543 independent reflexions up to θ = 30°. A four-circle diffractometer, equipped with Mo *K*α radiation (λ = 0.71069 Å), and an ω/2θ scan

technique were used. An absorption correction was made using the *ORABS* program (Schwarzenbach, 1972). 1402 reflexions were considered as observed by the criterion *I* > 2σ(*I*) and used in the remaining calculations.

The structure was solved by the multiresolution tangent-formula program *MULTAN* (Main, Lessinger, Woolfson, Germain & Declercq, 1977) and successive Fourier syntheses. Scattering factors for neutral atoms and anomalous-dispersion corrections for S were taken from *International Tables for X-ray Crystallography* (1974). The H atoms were located on a difference map calculated after least-squares refinement. The last cycles of anisotropic refinement (isotropically fixed H atoms) were performed using a weighting scheme of type *w* = *w*₁ · *w*₂, where *w*₁ = 1/(*a* + *b*|*F*_o|)² and *w*₂ = 1/(*c* + *d* sin θ/λ). Final disagreement indices are *R* = 0.046 and *R*_w = 0.048. Table 1 shows the atomic parameters.*

* Lists of coefficients for the weighting scheme, structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36798 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.