N1-C5-C10	133.8 (2)	C16-N15-S2	126.2 (2)
C13-C10-C5	117.5 (2)	C21-C16-C17	122.5 (2)
C13-C10-C24	110.8 (2)	C17-C16-N15	107.1 (2)
C5-C10-C24	109.0 (2)	C18-C17-C16	118.5 (2)
C13-C10-C11	109.1 (2)	C16-C17-C13	107.8 (2)
C5-C10-C11	98.5 (2)	C20-C21-C16	117.3 (2)
C24C10C11	111.4 (2)	C26-C25-S1	119.6 (2)
C12-C11-C10	110.2 (2)	C30-C25-S1	118.8 (2)
C4C12C23	112.2 (2)	C32-C31-C36	120.5 (3)
C4C12C22	110.7 (2)	C36-C31-S2	120.1 (2)
C23-C12-C22	109.9 (2)		
01-\$1-N1-C2	158.0(2)	C12-C4-C5-C10	-5.2 (2)
02-S1-N1-C2	28.0 (2)	C5-C10-C11-C12	-16.8 (2)
C25-S1-N1-C2	-87.0(2)	C3-C4-C12-C22	-56.6 (3)
N1-S1-C25-C26	53.6 (2)	C3-C4C12C23	66.6 (3)
O3-S2-N15-C16	-171.5(2)	C11-C10-C13-C14	-114.8(2)
O4-S2-N15-C16	-41.5 (2)	C10-C13-C14-N15	172.9 (2)
C31-S2-N15-C16	73.3 (2)	N1-C5-C10-C24	59.0 (2)
N15-S2-C31-C32	87.0(2)	N1-C5-C10-C11	175.2 (2)

For both compounds, data collection: *CAD-4 Software* (Enraf-Nonius, 1989); cell refinement: *CELSIUS* (Svenson, 1974); data reduction: *CORINC* (Dräger & Gattow, 1971; Wiehl & Schollmeyer, 1994). Program(s) used to solve structures: *SHELXS86* (Sheldrick, 1990) for (1); *SIR92* (Altomare *et al.*, 1994) for (2). For both compounds, program(s) used to refine structures: *SHELXL93* (Sheldrick, 1993); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL93*.

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Lists of structure factors, anisotropic displacement parameters, Hatom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1009). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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# A Thyrotropin-Releasing Hormone Analogue: pGlu-Phe-D-Pro- $\Psi$ [CN<sub>4</sub>]-NMe at 293 and 107 K

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# Abstract

Data have been measured at two temperatures, 293 K and 107 K, for a crystal of a thyrotropinreleasing hormone analogue, pGlu-Phe-D-Pro- $\Psi$ [CN<sub>4</sub>]-NMe, C<sub>20</sub>H<sub>25</sub>N<sub>7</sub>O<sub>3</sub>, and the structures solved and refined. The tripeptide contains a tetrazole ring which mimics a *cis*-peptide bond at the C terminus. An intermolecular hydrogen bond exists between two molecules related by the twofold screw axis, resulting in infinite chains of hydrogen-bonded peptide molecules. Because of the folding and packing of the molecules, there are no intermolecular contacts of less than 4 Å to the N atom of the phenylalanine residue.

# Comment

The title compound was prepared by solution methods in an ongoing evaluation of the 1,5-disubstituted tetrazole ring as a surrogate for *cis*-amide bonds (Marshall, Humblet, Van Opdenbosch & Zabrocki, 1981; Zabrocki, Smith, Dunbar, Iijima & Marshall, 1988; Smith, Zabrocki, Flak & Marshall, 1991; Zabrocki, Dunbar, Marshall, Toth & Marshall, 1992). The conformation of the peptide backbone is all *trans*. The tetrazole ring mimics a *cis*-peptide bond for atoms CA3—C3— N4—CA4. The proline residue has a D configuration with  $\varphi$  values of 125.9 and 124.6° for the 293 and 107 K structures, respectively. Schematic diagrams of the thyrotropin-releasing hormone, (I), and the analogue described in this paper, (II), are illustrated below.

> His L-Pro-NH2 **(I)** pGlu Phe D-Pro CH<sub>3</sub> pGlu CN<sub>4</sub>-NMe (II)

The refined N-H distances range from 0.835 to 0.861 Å, and 0.838 to 0.895 Å, while the C—H distances range from 0.889 to 1.012 Å, and 0.890 to 1.013 Å, for the 293 and 107 K structures, respectively. A complete listing of bond distances is provided in the supplementary material. No intramolecular hydrogen bonds exist and only the pGlu residue participates in the intermolecular hydrogen-bonding scheme. The H atom of N1 is donated to a symmetry-related carbonyl O atom (OE1) and because of the presence of the twofold screw axis. infinite chains of hydrogen-bonded peptide molecules are produced parallel to the b axis, as illustrated in Fig. 1. Donor-acceptor hydrogen-bond distances are 2.809 (2) and 2.803 (2) Å, and hydrogen-acceptor distances are 1.952(15) and 1.912(18) Å for the 273 and 107 K structures, respectively; the respective  $D - H \cdots A$ 

angles are 174.5 (14) and 173.7 (16)°.



Fig. 1. Packing diagram for the 107 K structure showing the hydrogenbond network. The packing of the molecules in the two structures is identical.

Fig. 2. *ORTEPII* drawings (Johnson, 1976) of the (*a*) 293 K and (*b*) 107 K structures with all non-H atoms labelled. Displacement ellipsoids are drawn at 50% probability, and H atoms have been assigned an isotropic temperature factor of 1.0 Å<sup>2</sup> for clarity.

An unusual situation exists in that the N atom of the phenylalanine residue does not participate in any hydrogen bonding. It makes no intramolecular contacts to a potential hydrogen-bond acceptor and the shortest distance to a symmetry-related molecule is 3.98 Å (CD3 of proline).

The largest r.m.s. deviation of an atom from the leastsquares planes defining the phenylalanine and tetrazole rings is 0.005 at 293 K and 0.003 Å at 107 K. ORTEPII drawings (Johnson, 1976) of the 293 and 107 K structures are illustrated in Fig. 2.

# **Experimental**

Single crystals of the thyrotropin-releasing hormone analogue pGlu-Phe-D-Pro- $\Psi$ [CN<sub>4</sub>]-NMe were grown by slow evaporation of ethanol. The same crystal was used to collect both sets of data at 293 and 107 K.

#### Compound at 293 K

Crystal data

	Mo $K\alpha$ radiation
$M_r = 411.47$	$\lambda = 0.71069 \text{ Å}$
Monoclinic	Cell parameters fro
<i>P</i> 2 <sub>1</sub>	reflections
a = 13.464(1)Å	$\theta = 9.96 - 14.05^{\circ}$
b = 6.225(1) Å	$\mu = 0.0905 \text{ mm}^{-1}$
c = 13.476(1)  Å	T = 293  K
$\beta = 118.52^{\circ}$	Plate
$V = 992.2 (1) \text{ Å}^3$	0.6 imes 0.4 imes 0.08 is
Z = 2	Colorless
$D_x = 1.377 \text{ Mg m}^{-3}$	

Data collection

Syntex P3 diffractometer			
$\theta/2\theta$ scans			
Absorption correction:			
none			
5758 measured reflections			
3901 independent reflections			
3901 observed reflections			
$R_{int} = 0.016$			

#### Refinement

Refinement on F R = 0.057wR = 0.034S = 1.6533901 reflections 370 parameters All H-atom parameters refined  $w = 1/\sigma^2(F)$ 

# Compound at 107 K

Crystal data  $C_{20}H_{25}N_7O_3$  $M_r = 411.47$  om 49 mm

 $\theta_{\rm max} = 32.48^{\circ}$  $h = -20 \rightarrow 17$  $k = 0 \rightarrow 9$  $l = 0 \rightarrow 20$ 6 standard reflections monitored every 60 reflections intensity decay: 2%

 $(\Delta/\sigma)_{\rm max} = 0.06$  $\Delta \rho_{\rm max} = 0.614 \ {\rm e} \ {\rm \AA}^{-3}$  $\Delta \rho_{\rm min} = -0.436 \ {\rm e} \ {\rm \AA}^{-3}$ Extinction correction: none Atomic scattering factors from International Tables for X-ray Crystallography (1974, Vol. IV)

Mo  $K\alpha$  radiation

 $\lambda = 0.71069 \text{ Å}$ 

a = 13.397 (1) Å b = 6.171 (1) Åc = 13.331 (1) Å  $\beta = 118.44 \ (1)^{\circ}$ Plate V = 969.1 (3) Å<sup>3</sup>

#### Data collection

 $D_x = 1.410 \text{ Mg m}^{-3}$ 

Monoclinic

 $P2_1$ 

Z = 2

Syntex P3 diffractometer  $\theta/2\theta$  scans Absorption correction: none 3042 measured reflections 2440 independent reflections 2440 observed reflections  $R_{\rm int} = 0.023$ 

#### Refinement

Refinement on F R = 0.033wR = 0.032S = 1.8282440 reflections 370 parameters All H-atom parameters refined  $w=1/\sigma^2(F)$ 

Cell parameters from 49 reflections  $\theta = 9.96 - 14.05^{\circ}$  $\mu = 0.0926 \text{ mm}^{-1}$ T = 107 K $0.6 \times 0.4 \times 0.08 \text{ mm}$ Colorless

 $\theta_{\rm max} = 27.49^{\circ}$  $h = -17 \rightarrow 15$  $k = 0 \rightarrow 8$  $l = 0 \rightarrow 17$ 6 standard reflections monitored every 60 reflections intensity decay: <1%

 $(\Delta/\sigma)_{\rm max} = 0.05$  $\Delta \rho_{\rm max} = 0.550 \text{ e } \text{\AA}^{-3}$  $\Delta \rho_{\rm min} = -0.410 \text{ e } \text{\AA}^{-3}$ Extinction correction: none Atomic scattering factors from International Tables for X-ray Crystallography (1974, Vol. IV)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (Å<sup>2</sup>) at 293 and 107 K

$U_{\text{eq}} = (1/3) \sum_{i} \sum_{j} U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j.$				
	x	у	Z	$U_{eq}$
293 K				
N1	0.38806 (12)	0.3552	-0.10802 (11)	0.0339 (5)
CAI	0.30619 (13)	0.1991 (4)	-0.18180 (13)	0.0309 (6)
CB1	0.19348 (14)	0.3249 (4)	-0.23223 (18)	0.0394 (7)
CG1	0.22868 (13)	0.5598 (4)	-0.21487 (14)	0.0330(6)
CD1	0.34935 (12)	0.5573 (4)	-0.12122 (13)	0.0311 (6)
OE1	0.40382 (10)	0.7143 (4)	-0.06772 (11)	0.0505 (5)
C1	0.32875 (12)	0.1112 (4)	-0.27443 (12)	0.0287 (5)
01	0.27076 (10)	-0.0340 (3)	-0.33542 (10)	0.0427 (5)
N2	0.41506 (10)	0.2001 (4)	-0.28442 (10)	0.0298 (5)
CA2	0.44294 (12)	0.1336 (4)	-0.37231 (12)	0.0295 (6)
CB2	0.39539 (14)	0.2859 (4)	-0.47334 (15)	0.0395 (7)
CG2	0.27086 (13)	0.3248 (4)	-0.51944 (13)	0.0330 (6)
CD21	0.23130 (16)	0.5162 (4)	-0.49868 (16)	0.0432 (8)
CE21	0.11636 (18)	0.5472 (5)	-0.53617 (18)	0.0511 (9)
CZ2	0.04014 (17)	0.3888 (5)	-0.59553 (18)	0.0542 (9)
CE22	0.07853 (16)	0.1995 (5)	-0.61815 (18)	0.0556 (8)
CD22	0.19268 (15)	0.1672 (4)	-0.58053 (15)	0.0447 (7)
C2	0.57183 (12)	0.1101 (4)	-0.31993 (13)	0.0314 (6)
02	0.62785 (9)	0.2380 (3)	-0.34166 (11)	0.0461 (5)
N3	0.61945 (10)	-0.0563 (4)	-0.24992 (11)	0.0348 (5)
CA3	0.74122 (14)	-0.0981 (4)	-0.20287 (15)	0.0368 (7)
CB3	0.75192 (16)	-0.3319 (4)	-0.1637 (2)	0.0495 (8)
CG3	0.65971 (18)	-0.3571 (5)	-0.13085 (19)	0.0504 (9)
CD3	0.56297 (16)	-0.2251 (5)	-0.2181 (2)	0.0517 (9)
C3	0.81055 (13)	0.0515 (4)	-0.10825 (14)	0.0333 (6)
N5	0.94282 (12)	0.2779 (4)	-0.00248 (13)	0.0480 (6)
N6	0.88790 (14)	0.2176 (4)	0.04932 (13)	0.0577 (8)
N7	0.80511 (14)	0.0759 (4)	-0.01431 (13)	0.0523 (7)
N4	0.89425 (10)	0.1749 (4)	-0.10261 (11)	0.0355 (5)
CA4	0.93656 (22)	0.2020(6)	-0.1828(2)	0.0615(12)

					a a. a.		
107 K					CAI = CI = OI	120.3(1)	120.2 (2)
N1	0.38697 (13)	0.3552	-0.10768 (12)	0.0178 (5)	CA1—C1—N2	116.9 (1)	117.1 (2)
CA1	0.30434 (14)	0.1973 (4)	-0.18197 (14)	0.0167 (6)	01—C1—N2	122.7 (1)	122.8 (2)
CB1	0 19123 (15)	0.3247(4)	-0.23200(17)	0.0205(7)	C1—N2—CA2	122.0(1)	121.7 (2)
CCI	0.17125(15)	0.5676 (4)	-0.21723 (15)	0.0203(1)	$N^2$ $CA^2$ $CB^2$	1127(1)	1124(2)
	0.22704 (14)	0.5020 (4)	-0.21723(13)	0.0177(0)	$N_2 CA2 C2$	109.0 (1)	108.9(2)
CDI	0.34819 (14)	0.5604 (4)	-0.12187(14)	0.0103 (0)	N2-CA2-C2	109.0(1)	108.7 (2)
OE1	0.40287 (10)	0.7188 (4)	-0.06859 (11)	0.0255 (5)	$CB2 \rightarrow CA2 \rightarrow CZ$	111.7(1)	111.5 (2)
C1	0.32729 (13)	0.1103 (4)	-0.27595 (14)	0.0156 (6)	CA2—CB2—CG2	112.2 (2)	111.8 (2)
01	0.26817 (11)	-0.0339(3)	-0.33878(10)	0.0217 (5)	CB2—CG2—CD21	121.0 (2)	120.8 (2)
N2	0.41509 (11)	0 1986 (4)	-0.28488(12)	0.0164 (5)	CG2-CD21-CE21	120.9 (2)	120.9 (2)
C42	0.41307 (11)	0.1305 (4)	-0.37320(13)	0.0160 (6)	CD21 - CF21 - C72	120 3 (2)	120.0 (2)
CAZ	0.44347(13)	0.1303 (4)	-0.37320(13)	0.0100 (0)	CE21 $CE21$ $CE2$	110.2 (2)	1104(2)
CB2	0.39010(15)	0.2849 (4)	-0.4/556(15)	0.0206 (7)		119.2 (2)	117.4 (2)
CG2	0.27078 (15)	0.3240 (4)	-0.52140 (14)	0.0185 (6)	CZ2=CE22=CD22	120.8 (2)	120.6 (2)
CD21	0.23140 (16)	0.5166 (4)	-0.49920 (15)	0.0221 (7)	CE22—CD22—CG2	120.7 (2)	120.5 (2)
CE21	0.11606 (16)	0.5478 (4)	-0.53612 (16)	0.0253 (7)	CD22—CG2—CD21	118.2 (2)	118.6 (2)
C72	0.03898 (16)	0 3865 (4)	-0 59659 (17)	0.0275 (8)	CD22—CG2—CB2	120.8 (2)	120.5 (2)
CED	0.07762 (16)	0.1047 (5)	0.62011 (16)	0.0277(7)	$C_{A2} = C_{2} = O_{2}$	121.2 (1)	121 4 (2)
CE 22	0.07702(10)	0.1947(3)	-0.02011 (10)	0.0277 (7)	02 C2 N3	121.0 (1)	122.1 (2)
CD22	0.19240(15)	0.1632 (4)	-0.58300 (15)	0.0230(7)	02 - 02 - 103	121.9(1)	122.1 (2)
C2	0.57290 (14)	0.1076 (4)	-0.31992 (14)	0.0170 (6)	CA2 = C2 = N3	116.9(1)	116.5 (2)
O2	0.62988 (10)	0.2381 (3)	-0.34071 (11)	0.0231 (5)	C2—N3—CA3	120.0(1)	119.9 (2)
N3	0.62002 (11)	-0.0612(4)	-0.24932(12)	0.0176 (5)	C2—N3—CD3	128.0 (2)	127.7 (2)
C43	0.74227(15)	0 1038 (4)	-0.20133(15)	0.0185 (6)	N3-CA3-CB3	102.6(2)	102.9 (2)
CAD	0.74227 (15)	0.1050 (4)	-0.20135 (13)	0.0105(0)	CA3_CB3_CG3	104.1 (2)	103.8 (2)
CBS	0.75314(15)	-0.3390 (4)	-0.10128 (17)	0.0244(7)		102.8 (2)	103.8 (2)
CG3	0.65914 (17)	-0.3628 (4)	-0.12827 (18)	0.0260 (7)	CB3-CG3-CD3	103.8 (2)	103.1 (2)
CD3	0.56169(15)	-0.2333 (4)	-0.22006 (17)	0.0252 (7)	CG3—CD3—N3	103.9 (2)	103.3 (2)
C3	0.81194 (14)	0.0481 (4)	-0.10585(15)	0.0177 (6)	CD3—N3—CA3	111.8 (2)	112.1 (2)
N5	0.94432 (13)	0 2770 (4)	-0.00040(13)	0.0242 (6)	N3—CA3—C3	111.8 (2)	111.8 (2)
NIC	0.00000 (13)	0.2145(4)	0.05207 (12)	0.0270 (6)	CB3_CA3_C3	1124(2)	1124(2)
IND	0.89088 (13)	0.2143 (4)	0.03397(13)	0.0279(0)		112.7 (2)	112.4 (2)
N7	0.80763 (13)	0.0710(4)	-0.00956 (13)	0.0258 (6)	CA3-C3-N4	125.0 (2)	124.9 (2)
N4	0.89471 (11)	0.1744 (4)	-0.10155 (12)	0.0182 (5)	CA3—C3—N7	126.6 (2)	126.6 (2)
CA4	0.93568 (18)	0.2036 (5)	-0.18413(18)	0.0294 (8)	C3—N4—CA4	130.1 (2)	130.2 (2)
				. ,	CA4N4N5	121.0 (2)	121.0 (2)
Table 2.	Selected	geometric i	parameters (Å	°) at 293	C3-N4-N5	1089(1)	108.8 (2)
	5000000			) ui 2))	NA N5 N6	105.9(1)	106.2 (2)
		and 107	′ K			103.9(1)	100.2 (2)
		202 12	107 1		N5-N6-N7	110.9 (2)	110.7 (2)
		293 K	107 K		N6—N7—C3	106.1 (2)	105.8 (2)
CA1 - N1		1.450 (2)	1.453 (2)		N7—C3—N4	108.2 (1)	108.4 (2)
N1-CD1		1.340 (2)	1.347 (2)		<b>T1</b> : 6		
CD10E1		1.228 (3)	1.225 (3)		The variance of ea	ch structure i	actor was calculated according
CDI-CGI		1 508 (2)	1 512 (2)		to the method of	Blessing (19)	87). The structure was solved
		1.500 (2)	1.578 (2)		in anoth anoth her	dinget meet	ada waina MILLTAN (Main
		1.520(3)	1.528 (5)		in each case by	unect metr	ious using MULIAN (Main,
CBI-CAI		1.547 (5)	1.348 (3)		Hull, Lessinger,	Germain, D	eclercq & Woolfson, 1978).
CAI-CI		1.521 (3)	1.523 (3)		Following anisotro	nio rafinama	nt of all non H atoms by full
C101		1.221 (3)	1.220 (3)		I onowing anisotic	pic remience	
C1—N2		1.351 (3)	1.352 (2)		matrix least squar	es, minimizir	ig $\Sigma w (F_o - F_c)^2$ , the positions
N2—CA2		1.463 (3)	1.461 (3)		of all protons w	ere determin	ed from a difference man
CA2 - CB2		1 526 (3)	1 530 (3)				ied from a difference map.
CB2 - CC2		1 504 (2)	1 508 (3)		Positional paramet	ers were ren	ned for all atoms; anisotropic
CD2 = CD2		1.304 (2)	1.300 (3)		displacement para	meters were	refined for all non-H atoms
C02-CD2	1	1.387 (3)	1.389 (3)				
CD21-CE2	21	1.393(3)	1 494 (4)		while icotropic di	nlocomont n	aromators wars refined for all
CE21—CZ2			1.574 (5)		while isotropic dis	splacement p	arameters were refined for all
CZ2-CE22		1.372 (4)	1.384 (3)		while isotropic dis H atoms. A $\delta(R)$	splacement p plot was cale	arameters were refined for all culated for both data sets and
		1.372 (4) 1.378 (4)	1.384 (3) 1.386 (4)		while isotropic dis H atoms. A $\delta(R)$	placement p plot was cald	arameters were refined for all culated for both data sets and 992). The slope and intercent
CE22—CD2	22	1.372 (4) 1.378 (4) 1.384 (3)	1.384 (3) 1.386 (4) 1.387 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel	splacement p plot was cald l & Smith, 1	arameters were refined for all culated for both data sets and 992). The slope and intercept
CE22—CD2 CD22—CG	22	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar	splacement p plot was cale l & Smith, 1 es line were	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and
CE22—CD2 CD22—CG2	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729 respectivel	splacement p plot was cald l & Smith, 1 es line were y for the 293	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and K data and 1.682 and 0.0441
CE22—CD2 CD22—CG2 CA2—C2 C2 O2	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel	splacement p plot was cald l & Smith, 1 es line were y, for the 293	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441,
CE22—CD2 CD22—CG2 CA2—C2 C2—O2	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—N3	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak
CE22—CD2 CD22—CG CA2—C2 C2—O2 C2—N3 N3—CD3	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CG3	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.386 (3) 1.224 (3) 1.224 (3) 1.340 (3) 1.476 (4) 1.514 (3)	1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from
CE22—CD2 CD22—CG CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CG3 CG3—CB3	22 2	1.372 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4)	1.384 (3) 1.384 (3) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation.	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CD3 CG3—CB3 CB3—CA3	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.514 (3) 1.513 (4) 1.531 (4)	1.384 (3) 1.384 (3) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4) 1.529 (4)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps	splacement p plot was cald l & Smith, l es line were y, for the 293 he 107 K da were reporte an H atom w r calculation.	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to many
CE22—CD2 CD22—CG CA2—C2 C2—O2 C2—N3 N3—CD3 CG3—CG3 CG3—CG3 CG3—CA3 CA3—CA3	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.386 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4)	1.384 (3) 1.384 (3) 1.386 (4) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4) 1.529 (4)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation. were similar	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps
CE22—CD2 CD22—CG CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CG3 CG3—CB3 CB3—CA3 CA3—N3 CA2—C2	22	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.547 (2) 1.514 (3) 1.513 (4) 1.513 (4) 1.531 (4) 1.471 (2)	1.384 (3) 1.384 (3) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4) 1.529 (4) 1.471 (2) 1.406 (2)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from higl	splacement p plot was cale l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation. were similar nly accurate e	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies.
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CC3 CG3—CC3 CG3—CC3 CA3—C3 CA3—C3	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3)	1.384 (3) 1.384 (3) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4) 1.529 (4) 1.471 (2) 1.496 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation, were similar nly accurate of	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies.
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—O2 C2—N3 N3—CD3 CD3—CG3 CB3—CA3 CA3—CA3 CA3—N3 CA3—C3 C3—N4	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3) 1.336 (3)	1.384 (3) 1.384 (3) 1.386 (4) 1.387 (3) 1.393 (3) 1.526 (2) 1.228 (3) 1.343 (3) 1.477 (3) 1.523 (3) 1.526 (4) 1.529 (4) 1.471 (2) 1.496 (3) 1.334 (3)		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation, were similar nly accurate e	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 6 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies.
CE22—CD2 CD22—CG2 CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CG3 CG3—CB3 CG3—CB3 CG3—CA3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 CA3—C3	22	1.372 (4) 1.378 (4) 1.378 (4) 1.386 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3) 1.336 (3) 1.452 (4)	$\begin{array}{c} 1.384 (3) \\ 1.387 (3) \\ 1.393 (3) \\ 1.526 (2) \\ 1.228 (3) \\ 1.523 (3) \\ 1.523 (3) \\ 1.522 (4) \\ 1.529 (4) \\ 1.529 (4) \\ 1.471 (2) \\ 1.496 (3) \\ 1.334 (3) \\ 1.456 (3) \end{array}$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high	splacement p plot was cale l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation were similar hly accurate o vould like	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies. to thank Trevor D. Smith
CE22—CD2 CD22—CC3 C22—C2 C2—O2 C2—N3 N3—CD3 CG3—CG3 CG3—CG3 CG3—CG3 CG3—CA3 CA3—N3 CA3—N3 CA3—N4 N4—CA4 N4—N5	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3) 1.348 (3) 1.452 (4) 1.348 (2)	$\begin{array}{c} 1.384 (3) \\ 1.384 (3) \\ 1.387 (3) \\ 1.393 (3) \\ 1.526 (2) \\ 1.228 (3) \\ 1.343 (3) \\ 1.477 (3) \\ 1.523 (3) \\ 1.526 (4) \\ 1.529 (4) \\ 1.471 (2) \\ 1.496 (3) \\ 1.334 (3) \\ 1.456 (3) \\ 1.345 (2) \end{array}$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high The authors v for technical assi	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation. were similar nly accurate of vould like	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies.
CE22—CD2 CD22—CC3 CA2—C2 C2—O2 C2—O2 C2—N3 N3—CD3 CD3—CC3 CB3—CA3 CA3—CA3 CA3—CA3 CA3—CA3 CA3—CA3 CA3—CA4 N4—CA4 N4—N5 N5—N6	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3) 1.336 (3) 1.452 (4) 1.348 (2) 1.291 (3)	$\begin{array}{c} 1.384 (3) \\ 1.384 (3) \\ 1.387 (3) \\ 1.393 (3) \\ 1.526 (2) \\ 1.228 (3) \\ 1.343 (3) \\ 1.477 (3) \\ 1.523 (3) \\ 1.526 (4) \\ 1.529 (4) \\ 1.529 (4) \\ 1.471 (2) \\ 1.496 (3) \\ 1.334 (3) \\ 1.345 (2) \\ 1.296 (3) \\ 1.296 (3) \end{array}$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high The authors v for technical assis	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation, were similar nly accurate of vould like istance with	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies. to thank Trevor D. Smith crystal growth. One of the
CE22—CD2 CD22—CC3 CA2—C2 C2—O2 C2—N3 N3—CD3 CD3—CC3 CG3—CB3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 CA3—C3 C3—N4 N4—CA4 N4—CA4 N4—N5 N5—N6 N6—N7	22	1.372 (4) 1.378 (4) 1.378 (4) 1.386 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.492 (3) 1.336 (3) 1.452 (4) 1.348 (2) 1.291 (3) 1.357 (3)	$\begin{array}{c} 1.384 (3) \\ 1.387 (3) \\ 1.393 (3) \\ 1.526 (2) \\ 1.228 (3) \\ 1.526 (3) \\ 1.523 (3) \\ 1.523 (3) \\ 1.526 (4) \\ 1.529 (4) \\ 1.529 (4) \\ 1.471 (2) \\ 1.496 (3) \\ 1.334 (3) \\ 1.345 (2) \\ 1.296 (3) \\ 1.358 (3) \end{array}$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high The authors v for technical assis authors (JZ) acl	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation were similar hly accurate of vould like istance with knowledges	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies. to thank Trevor D. Smith crystal growth. One of the financial support for part
CE22—CD2 CD22—CC3 C22—C2 C2—O2 C2—N3 N3—CD3 CG3—CG3 CG3—CG3 CG3—CG3 CG3—CG3 CG3—CA3 CA3—N3 CA3—N4 N4—CA4 N4—N5 N5—N6 N6—N7 N7—C3	22	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.547 (2) 1.513 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.471 (2) 1.492 (3) 1.336 (3) 1.452 (4) 1.348 (2) 1.291 (3) 1.357 (3) 1.311 (3)	$\begin{array}{c} 1.384 (3) \\ 1.384 (3) \\ 1.387 (3) \\ 1.393 (3) \\ 1.526 (2) \\ 1.228 (3) \\ 1.343 (3) \\ 1.523 (3) \\ 1.526 (4) \\ 1.529 (4) \\ 1.529 (4) \\ 1.471 (2) \\ 1.496 (3) \\ 1.334 (3) \\ 1.456 (3) \\ 1.345 (2) \\ 1.296 (3) \\ 1.358 (3) \\$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high The authors v for technical assi authors (JZ) act of this work for	splacement p plot was cale 1 & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation. were similar ily accurate of vould like istance with cnowledges	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, ata. Minimum and maximum d as the fraction of a peak hich had been excluded from The appearance of the final in many respects to maps electron-density studies. to thank Trevor D. Smith crystal growth. One of the financial support for part a Committee for Socientific
CE22—CD2 CD22—CC3 CA2—C2 C2—O2 C2—O2 C2—N3 N3—CD3 CD3—CC3 CB3—CA3 CA3—CA3 CA3—CA3 CA3—CA3 CA3—CA3 CA3—CA4 N4—CA4 N4—N5 N5—N6 N6—N7 N7—C3	22 2	1.372 (4) 1.378 (4) 1.378 (4) 1.384 (3) 1.386 (3) 1.537 (2) 1.224 (3) 1.340 (3) 1.476 (4) 1.513 (4) 1.513 (4) 1.513 (4) 1.531 (4) 1.471 (2) 1.492 (3) 1.336 (3) 1.452 (4) 1.348 (2) 1.291 (3) 1.357 (3) 1.311 (3)	$\begin{array}{c} 1.384\ (3)\\ 1.384\ (3)\\ 1.387\ (3)\\ 1.393\ (3)\\ 1.526\ (2)\\ 1.228\ (3)\\ 1.477\ (3)\\ 1.523\ (3)\\ 1.523\ (3)\\ 1.526\ (4)\\ 1.529\ (4)\\ 1.529\ (4)\\ 1.471\ (2)\\ 1.496\ (3)\\ 1.334\ (3)\\ 1.345\ (2)\\ 1.296\ (3)\\ 1.358\ (3)\\ 1.320\ (3)\\ \end{array}$		while isotropic dis H atoms. A $\delta(R)$ was linear (Howel of the least-squar 0.1729, respectivel respectively, for t difference peaks corresponding to a the structure-facto difference maps obtained from high The authors v for technical assis authors (JZ) ach of this work from	splacement p plot was cald l & Smith, 1 es line were y, for the 293 he 107 K da were reporte an H atom w r calculation, were similar nly accurate of vould like istance with knowledges om the State	arameters were refined for all culated for both data sets and 992). The slope and intercept calculated to be 1.558 and 8 K data and 1.682 and 0.0441, tta. Minimum and maximum d as the fraction of a peak hich had been excluded from . The appearance of the final in many respects to maps electron-density studies. to thank Trevor D. Smith crystal growth. One of the financial support for part e Committee for Scientific
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CB1-CA1-C1

NI-CAI-CI

111.1 (1)

114.8 (1)

111.4 (2)

114.2 (1)

Square, Chester CH1 2HU, England.

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# *trans*-3-(*p*-Chlorophenylthio)-1,4,6-trimethylpiperazine-2,5-dione

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#### Abstract

The title compound,  $C_{13}H_{15}CIN_2O_2S$ , assumes a shallow boat conformation where the methyl and 4-chlorothiophenyl substituents in the  $\alpha$ -positions are situated *trans* to one another, and the latter is folded across the piperazinedione ring.

### Comment

As part of our continuing studies on piperazinediones (Chai & Page, 1993; Chai, King & Hockless, 1995), the structure of the title compound (I) was undertaken to establish the relative stereochemistry of the substituents at the C<sup> $\alpha$ </sup> positions. The crystal structure reveals a shallow boat conformation [ $\beta = -10.95^{\circ}$  in the Hooker notation, defined as the dihedral angle between the two amide planes C(3)—C(2)—N(1)—C(6) and C(3)—N(4)—C(5)—C(6)] (Hooker, Bayley, Radding & Schell-

man, 1974) with the thiophenyl ligand occupying a pseudo-axial position, and the methyl C atom pseudo-equatorial.



Conformational parameters (in accord with the IUPAC-IUB Commission on Biochemical Nomenclature, 1970) were calculated as follows:  $\omega_1$  [C(3)— C(2)—N(1)—C(6)] = 8.1 (4),  $\psi_1$  [N(1)—C(6)—C(5)— N(4)] = 5.5 (3),  $\varphi_1$  [C(2)—N(1)—C(6)—C(5)] = 0.0 (4),  $\omega_2$  [C(6)—C(5)—N(4)—C(3)] = -20.1 (3),  $\psi_2$  [N(4)— C(3)—C(2)—N(1)] = -20.8 (3),  $\varphi_2$  [C(5)—N(4)— C(3)—C(2)] = 27.7 (3)°. Although bond lengths and angles are generally as expected, the significant differences in equivalent torsion angles suggest a substantial twist in conformation, which presumably reflects some flexibility in the molecule, enabling it to rotate and deform in order to minimize any unfavourable intramolecular interactions. Like other compounds of this type containing phenyl substituent side chains



Fig. 1. View of the title compound showing the labelling of all non-H atoms. Displacement ellipsoids are shown at 50% probability levels. H atoms are drawn as circles of arbitrary radii.