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The hydrogen-bonding network in (+)-*N*-tosyl-L-glutamic acid

Janusz Zachara,* Izabela Madura, Halina Hajmowicz and Ludwik Synoradzki

Warsaw University of Technology, Faculty of Chemistry, Noakowskiego 3, 00-664 Warszawa, Poland
Correspondence e-mail: janzac@ch.pw.edu.pl

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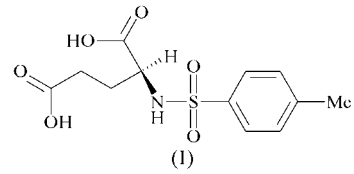
The asymmetric unit of the α polymorph of (+)-*N*-tosyl-L-glutamic acid, $C_{12}H_{15}NO_6S$, contains two independent molecules which differ in conformation. The carboxylic acid groups form an infinite zigzag chain with characteristic $R_2^2(8)$ rings running along the *b* axis. Intermolecular N—H···O and C—H···O contacts mediate the formation of a three-dimensional supramolecular structure described by $R_4^3(22)$, $R_6^6(44)$ and $R_8^8(54)$ graph-set descriptors. Comparison of the extended structure with that of *N*-(benzenesulfonyl)glutamic acid shows that a subtle difference in the periphery of the molecule, *i.e.* the replacement of the toluyl group with a phenyl group, can be accompanied by dramatic changes in molecular assembly.

Comment

Among naturally occurring amino acids of biological importance, aspartic and glutamic acid and their derivatives are characterized by the presence of two carboxylic acid groups, which make them interesting supramolecular synthons due to their ability to form moderate-to-strong hydrogen bonds (Jeffrey, 1997). (+)-*N*-Tosyl-L-glutamic acid, (I), is a commonly used reagent for separating racemates into optically active enantiomers. Nevertheless, its crystal structure has not been reported to date. The co-crystal of (I) and 5-bromocytosine has been characterized (Ohki *et al.*, 1976). Our previous studies showed that (I) crystallizes as α and β polymorphs. We present here the structure analysis of the stable α form of (I). The β polymorph crystallizes in the form of very thin needles; attempts to grow a crystal suitable for X-ray studies have not yet been fruitful.

The α form of (I) crystallizes in space group $P2_12_12_1$ with two independent molecules (*A* and *B*) in the asymmetric unit. The molecules are chiral and both exhibit the *S* configuration. Perspective views of molecules *A* and *B*, with the atom-numbering schemes, are depicted in Fig. 1. The bond lengths in the two molecules are the same to within 3σ, while the bond angles differ by less than 3.5°. However, a substantial discrepancy is observed between corresponding torsion angles (Table 1). This feature is the result of the hydrogen-bond network (see



(I)

below), which causes a divergence of the molecular environment (Steiner, 2002). The most significant conformational differences are observed for the orientation of the toluyl and one of the carboxyl groups in relation to the sulfonyl group. The different conformations of the two molecules are caused by twisting about the C—S and C—$C_{carboxyl}$ bonds, as seen in a comparision of the C11—C6—S1—N1 and C31—C26—S2—N2 torsion angles, which have values of 50.2 (3) and 93.9 (2)°, respectively, and O1—C1—C2—N1 and O21—C21—C22—N2, with values of 81.5 (3) and 175.4 (2)°, respectively. The torsion angles describing the positioning of the glutamic acid carbon chain in relation to the *N*-tosyl group are approximately the same for both molecules. Furthermore, the mutual

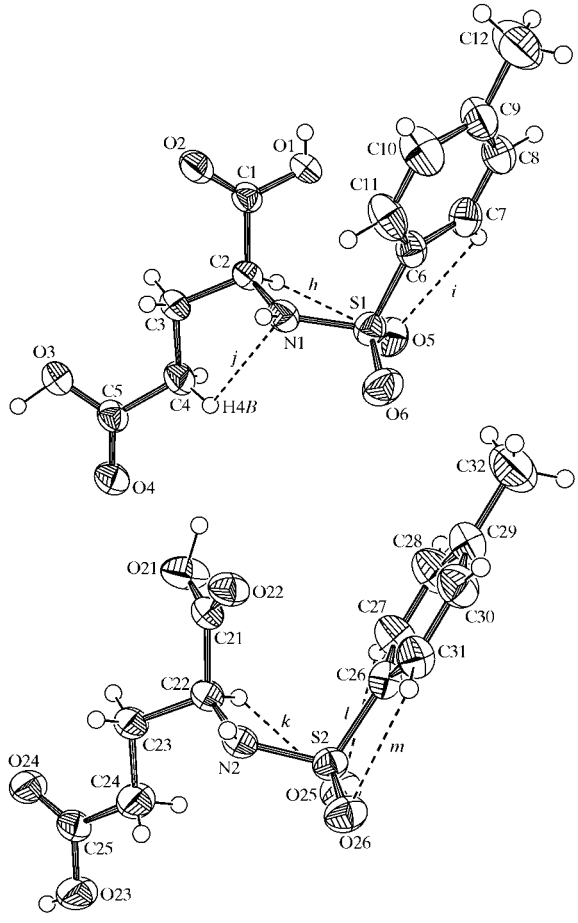


Figure 1
Molecules *A* (top) and *B* of (I), with the atom-numbering schemes, showing the difference in their conformations. The intramolecular hydrogen bonds with assigned graph-set motifs are also included. Displacement ellipsoids are drawn at the 50% probability level.

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orientation of the carboxyl groups in molecule *A* is different from that in *B*. The planes defined by the carboxyl groups form a dihedral angle of 25.3 (2)° in *A* and 39.9 (2)° in *B*.

Taking into account the differences between the two molecules, the hydrogen-bond network has been carefully analysed (Table 2). The strongest hydrogen bonds are observed between the carboxylic acid groups of molecules *A* and *B* (mean H···O and O···O distances of 1.81 and 2.67 Å, respectively), generating a one-dimensional zigzag chain with classical double hydrogen bonds. This pattern can be described by four discrete motifs (*a*, *b*, *c* and *d*; Fig. 2) (Etter, 1990; Bernstein *et al.*, 1995). The second-level graph [$N_2(ab)$ and $N_2(cd)$] depicts characteristic $R_2^2(8)$ rings, which combine to form an alternating infinite chain running along the *b* axis (Fig. 2). A complete set of binary graph-set descriptors is given in Table 3.

A totally different molecular arrangement was identified in the analogous glutamic acid derivative (−)-(*R*)-*N*-benzenesulfonylglutamic acid (Shan & Huang, 1999), where carboxylic groups are connected by single O—H···O bridges to form an open-chain $C(8)$ motif.

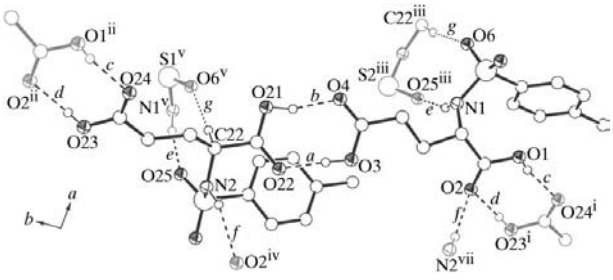

Figure 2
A plot showing the intermolecular hydrogen bonds in the structure of (I), with the assigned graph-set motifs. For clarity, the moieties of symmetry-related molecules are depicted in grey.

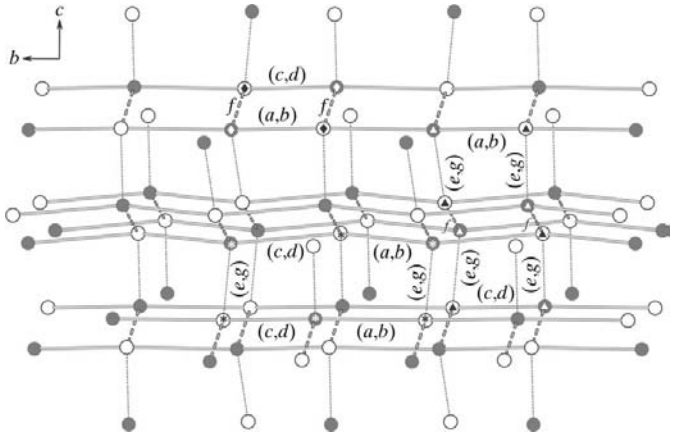

Figure 3
The hydrogen-bonded framework generated by the pseudo-tetrahedral supramolecular connections in (I). Molecules *A* and *B* are shown by open and filled circles, respectively, representing the centres of gravity of the molecules. Double carboxylic acid hydrogen bonds are depicted by solid lines. The connections *via* motifs *e* (and *g*) and *f* are denoted by dotted and dashed lines, respectively. The selected four-, six- and eight-membered rings are indicated by diamonds, asterisks and triangles, respectively.

The hydrogen-bond network in α-(I) further extends into the second dimension as the N1—H1N group of *A* forms a hydrogen bond with atom O25^{iii} of the sulfonyl group of *B* (motif *e*) [symmetry code: (iii) $\frac{1}{2}+x, \frac{3}{2}-y, 1-z$]. Moreover, motif *e*, together with the C22—H22···O6^{v} hydrogen bond (motif *g*) [symmetry code: (v) $x-\frac{1}{2}, \frac{3}{2}-y, 1-z$], forms a pattern with an $R_2^2(9)$ second-level graph-set descriptor. The $R_2^2(9)$ rings are almost perpendicular to the doubly hydrogen-bonded rings of the main chains (Fig. 2). The neighbouring atom O26 does not form a hydrogen bond, but is instead engaged in a weak intramolecular contact with C31—H31 as donor (Fig. 1). Additionally, the orientation of the sulfonyl group in molecule *B* enables the formation of an intramolecular contact between the second α-C atom (C27) of the toluyl group and O25, while in the case of *A* only the corresponding C7—H7···O5 grouping occurs. In the two molecules, the matching O5 and O25 atoms are also linked to C2—H2 and C22—H22 donors, respectively, to form weak intramolecular contacts. In addition, a C4—H4*B*···N1 contact is present in molecule *A* (Fig. 1). Furthermore, atom O2 acts as an acceptor in the hydrogen bonds O23—H23···O2^{ii} and N2—H2N···O2^{iv} (motifs *d* and *f* in Fig. 2) [symmetry codes: (ii) $x, 1+y, z$; (iv) $1-x, \frac{1}{2}+y, \frac{3}{2}-z$], mediating a well formed three-dimensional supramolecular structure.

Each *A* molecule is connected *via* hydrogen bonds to four *B* molecules and *vice versa*. The resulting three-dimensional network is shown in Fig. 3 in a simplfied form, in which the molecules are represented by their centres of gravity. The observed zigzag chain (parallel to the [010] direction) with hydrogen-bonded carboxylic acid groups of molecules *A* and *B* can be treated as the main building block, with each molecule acting as a pseudo-tetrahedral centre (contacts are represented by the solid lines linking the open and filled circles in Fig. 3). The chains are connected *via e* and *g* motifs (dotted lines in Fig. 3) into ribbons of fused six-membered chair rings. Neighbouring ribbons are connected through four-membered rings involving motif *f* (denoted by dashed lines in Fig. 3), to give channels with an eight-membered ring window. The four- and six-membered rings appear in the third-level graph set as $R_4^3(22)$ and $R_6^6(44)$, respectively. The eight-membered rings contain four motifs (*a*, *c*, *e* and *f*), so the descriptor is $N_4 = R_8^8(54)$.

In conclusion, we have demonstrated that the crystal structure of the title glutamic acid derivative, (I), is an interesting example of the ability of dicarboxylic acids to form extended supramolecular structures. Comparison of the structure of (I) with that of *N*-(benzenesulfonyl)glutamic acid shows that a subtle difference in the periphery of the molecule, *i.e.* the replacement of the toluyl group with a phenyl group, can be accompanied by dramatic changes in molecular assembly.

Experimental

The preparation and purification of (I) were reported previously by Hajmowicz *et al.* (1997). Single crystals of the α form of (I) were obtained by recrystallization from hot water by slow cooling to 273 K, with occasional stirring.

Crystal data

$C_{12}H_{15}NO_6S$
M_r = 301.32
Orthorhombic, $P2_12_12_1$
a = 9.2411 (9) Å
b = 16.934 (2) Å
c = 17.9235 (18) Å
V = 2804.8 (5) Å^3
Z = 8
D_x = 1.427 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 30 reflections
θ = 10–30°
μ = 0.26 mm^{-1}
T = 293 (2) K
Prism, white
0.4 × 0.3 × 0.2 mm

Data collection

Siemens $P3$ diffractometer
Profile data from $\omega/2\theta$ scans
2810 measured reflections
2810 independent reflections
2580 reflections with $I > 2\sigma(I)$
θ_{max} = 25.1°
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 20$
$l = 0 \rightarrow 21$
2 standard reflections
every 70 reflections
intensity decay: 1.8%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.028
$wR(F^2)$ = 0.075
S = 1.05
2810 reflections
416 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0463P)^2 + 0.3998P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0037 (5)
Absolute structure: Flack (1983)
Flack parameter: 0.04 (8)

Table 1
Selected geometric parameters (Å, °).

S1—N1	1.626 (2)	S2—N2	1.628 (2)
N1—C2	1.463 (3)	N2—C22	1.460 (4)
O1—C1	1.294 (3)	O21—C21	1.289 (4)
O2—C1	1.222 (3)	O22—C21	1.224 (3)
O3—C5	1.302 (4)	O23—C25	1.300 (4)
O4—C5	1.221 (3)	O24—C25	1.212 (4)
C2—N1—S1	123.79 (19)	C22—N2—S2	120.70 (18)
O2—C1—O1	124.5 (3)	O22—C21—O21	125.4 (3)
O4—C5—O3	123.5 (3)	O24—C25—O23	124.1 (3)
C6—S1—N1—C2	79.3 (2)	C26—S2—N2—C22	65.3 (2)
S1—N1—C2—C1	−86.6 (3)	S2—N2—C22—C21	−93.5 (2)
O1—C1—C2—N1	81.5 (3)	O21—C21—C22—N2	175.4 (2)
N1—S1—C6—C11	50.2 (3)	N2—S2—C26—C31	93.9 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O22	0.94 (3)	1.70 (3)	2.642 (3)	177 (5)
O21—H21···O4	0.95 (5)	1.72 (5)	2.654 (3)	164 (5)
O1—H1···O24^{i}	0.75 (3)	1.91 (3)	2.645 (3)	168 (4)
O23—H23···O2^{ii}	0.82 (5)	1.91 (5)	2.729 (3)	177 (7)
N1—H1N···O25^{iii}	0.86 (3)	2.23 (3)	3.053 (3)	160 (3)
N2—H2N···O2^{iv}	0.88 (3)	2.29 (3)	3.129 (3)	162 (2)
C22—H22···O6^{v}	1.05 (3)	2.27 (3)	3.308 (3)	171 (2)
C2—H2···O5	1.00 (3)	2.49 (3)	2.993 (3)	110 (2)
C7—H7···O5	0.93	2.59	2.946 (4)	103
C4—H4B···N1	0.97	2.51	2.933 (4)	106
C22—H22···O25	1.05 (3)	2.58 (3)	2.992 (3)	103 (2)
C27—H27···O25	0.93	2.66	2.977 (4)	101
C31—H31···O26	0.93	2.56	2.926 (3)	104

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

The positions and isotropic displacement parameters of H atoms attached to nitrogen and oxygen were refined freely. Methyl groups were modelled as idealized disordered rotating groups with refined occupancy factors [0.65 (5) and 0.64 (4) for the major conformers in molecules *A* and *B*, respectively]. The positions of the remaining H atoms were geometrically optimized and they were allowed to ride on their parent atoms with U_{iso}(H) values refined. The absolute structure was determined using the Flack parameter (Flack, 1983; Flack & Bernardinelli, 1999, 2000), the refined value of which, 0.04 (8), confirmed the already known *S* configuration of both molecules.

Data collection: *P3*/*P4-PC Software* (Siemens, 1991); cell refinement: *P3*/*P4-PC Software*; data reduction: *XDISK* (Siemens, 1991); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA1112). Services for accessing these data are described at the back of the journal.

Table 3
Graph-set matrix of unitary motifs (on-diagonal) and second-level patterns (off-diagonal) for (+)-*N*-tosyl-L-glutamic acid, (I).

Motif	*a*	*b*	*c*	*d*	*e*	*f*	*g*	*h*	*i*	*j*	*k*	*l*	*m*
a	$D(2)$												
b	$R_2^2(8)$	$D(2)$											
c	$C_2^2(16)$	$C_2^2(16)$	$D(2)$										
d	$C_2^2(16)$	$C_2^2(16)$	$R_2^2(8)$	$D(2)$									
e	$C_2^2(14)$	$C_2^2(14)$	$C_2^2(14)$	$C_2^2(14)$	$D(2)$								
f	$C_2^2(13)$	$C_2^2(13)$	$C_2^1(9)$	$C_2^2(11)$	$C_2^2(9)$	$D(2)$							
g	$C_2^2(13)$	$C_2^2(13)$	$C_2^2(13)$	$C_2^2(13)$	$R_2^2(9)$	$C_2^2(10)$	$D(2)$						
h	$D_2^2(9)$	$D_2^2(9)$	$D_2^2(7)$	$D_2^2(7)$	$D_2^2(6)$	$D_2^2(7)$	$D_2^2(7)$	$S(5)$					
i	$D_2^2(12)$	$D_2^2(12)$	$D_2^2(10)$	$D_2^2(10)$	$D_2^2(7)$	$D_2^2(10)$	$D_2^2(7)$	$R_2^1(8)$	$S(5)$				
j	$D_2^2(7)$	$D_2^2(7)$	$D_2^2(8)$	$D_2^2(8)$	$D_2^2(5)$	$D_2^2(8)$	$D_2^2(7)$	$R_2^2(8)$	$D_2^2(7)$	$S(5)$			
k	$D_2^2(7)$	$D_2^2(7)$	$D_2^2(9)$	$D_2^2(9)$	$R_2^1(5)$	$D_2^2(6)$	$D_1^2(4)$	†	†	†	$S(5)$		
l	$D_2^2(10)$	$D_2^2(10)$	$D_2^2(12)$	$D_2^2(12)$	$D_2^1(5)$	$D_2^2(7)$	$D_2^2(8)$	†	†	†	$R_2^1(8)$	$S(5)$	
m	$D_2^2(10)$	$D_2^2(10)$	$D_2^2(12)$	$D_2^2(12)$	$D_2^2(7)$	$D_2^2(7)$	$D_2^2(8)$	†	†	†	$R_2^2(8)$	$D_2^2(7)$	$S(5)$

† No link at binary level.

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