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# X-ray crystal structure of 2,5-dioxo-4-imidazolidineethanesulfonamide, $C_5H_9N_3O_4S$

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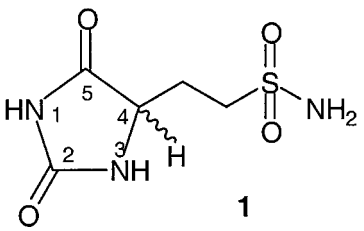
The crystal structure of 2,5-dioxo-4-imidazolidineethanesulfonamide or homocysteine sulfonamide hydantoin, $C_5H_9N_3O_4S$ (**1**) was obtained by single-crystal X-ray diffraction. Crystallization of **1** occurs in the centrosymmetric monoclinic space group $C2/c$ (No. 15) with $a = 15.653(2)$, $b = 9.6489(10)$, $c = 11.066(2)$ Å, $\beta = 94.64(2)^\circ$, and $Z = 8$. Molecules are in an extended structure with a C—C—C—S torsion angle of $-174.2(1)^\circ$. The imidazolidinedione ring is planar and the sulfonamide group has a distorted tetrahedral geometry. A three-dimensional network of intermolecular hydrogen bonding occurs within the crystal lattice involving both imidazolidinedione and sulfonamide functional groups.

**KEY WORDS:** Synthesis; crystal structure; hydrogen bonds; imidazolidine; sulfonamide; homocysteine; hydantoin; imidazolidinedione.

## Introduction

(*R*, *S*)-2,5-Dioxo-4-imidazolidineethanesulfonamide[2] or 5-(2-sulfamoylethyl)-2,4-imidazolidinedione, the hydantoin of D,L-homocysteine sulfonamide (3-amino-3-carboxypropanesulfonamide), is an analog of the amino acid glutamine in which both the amino and carboxyl functional groups are protected as the hydantoin (imidazolidinedione) and the side-chain carboxamide is replaced with the sulfonamide functional group (Scheme 1). Sulfonamides are commonly found in therapeutic agents and have been used to replace carboxamides in some substrates to make analogs that inhibit a number of enzyme-catalyzed reactions. Such analogs retain the potential to H-bond. 3-Amino-3-carboxypropanesulfonamide (homocysteine sulfonamide) acts as an inhibitor of both glutamine synthetase[1] and glutamate synthase.[2]




**1**

Scheme 1.

## Experimental

### *Synthesis*

The hydantoin of D,L-homocysteine sulfonamide, 2,5-dioxo-4-imidazolidineethanesulfonamide,

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[2] Separate numbering schemes are used for organic nomenclature and for the crystal structure.



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**Table 1.** Crystal Data and Structure Refinement

| | |
|---|---|
| Compound | $(C_3H_3N_2O_2)(CH_2)_2SO_2NH_2$ |
| CCDC deposit no. | CCDC-1003/6212 |
| Color/shape | clear-colorless/parallelepiped |
| Empirical formula | $C_5H_9N_3O_4S$ |
| Formula weight | 207.21 |
| Temperature, K | 293(2) |
| Crystal system | Monoclinic |
| Space group | $C2/c$ (No. 15) |
| Unit cell dimensions | $a = 15.653(2)$ Å<br>$b = 9.6489(10)$ Å<br>$c = 11.066(2)$ Å<br>$\beta = 94.64(2)^\circ$ |
| Volume, Å$^3$ | 1665.9(4) |
| $Z$ | 8 |
| Density (calculated), g/cm$^3$ | 1.652 |
| Absorption coefficient, mm$^{-1}$ | 0.376 |
| $\theta$ range for data collection, deg | 1.5–23.0 |
| Reflections measured | 2483 |
| Independent/observed reflections | 1158 ($R_{int} = 0.013$)/1026 ($[I > 2\sigma(I)]$) |
| Data/restraints/parameters | 1158/0/131 |
| Goodness of fit on $F^2$ | 1.092 |
| Final $R$ indices $[I > 2\sigma(I)]$ | $R_1 = 0.0264$, $wR_2 = 0.0747$ |
| $R$ indices (all data) | $R_1 = 0.0329$, $wR_2 = 0.0772$ |
| Extinction coefficient | 0.0060(7) |
| Max/min transmission | 0.999/0.981 |
| Largest diff. peak and hole | 0.228, −0.264 |

was prepared by modification of the method of Reisner.[3,4] D,L-Homocystine was first protected as the hydantoin, di-(2,4-imidazolidinedione-5-ethyl) disulfide,[5,6] then oxidatively chlorinated to give D,L-5-($\beta$-chlorosulfonylethyl)hydantoin. Liquid ammonia (150 mL) was condensed in a round bottom flask that contained 4.5 g (20 mmol) of D,L-5-($\beta$-chlorosulfonylethyl)hydantoin in a dry ice–acetone bath. The reaction was stirred until the reactant dissolved. The reaction flask was removed from the bath and ammonia was allowed to evaporate in the hood. The white, gummy product, D,L-homocysteine sulfonamide hydantoin, was recrystallized from hot water. Yield: 72%. M.pt. 185–186°C. Thin layer chromatography on silica gel with *n*-butanol/acetic acid/water (5/2/2) as eluent gave a single spot ($R_f$ 0.54) that was detected by treatment with chlorine gas followed by spraying with a solution of toluidine containing KI. One gram of the product was dissolved in boiling water, then filtered. The filtrate was stored in a refrigerator at 8°C for 1 week at which time crystals suitable for X-ray analysis were obtained.

### *Spectroscopy*

Infrared spectral data were collected on a Mattson Cygnus 100 FTIR analyzer using KBr pellets. Nuclear magnetic resonance spectra

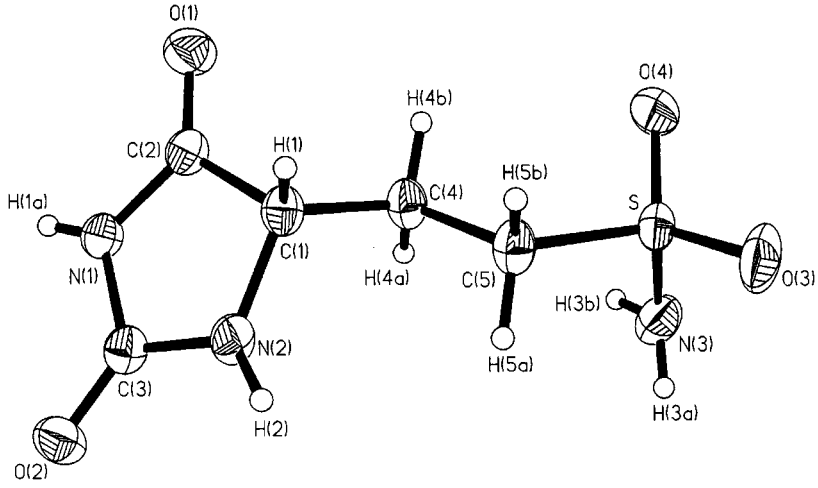


**Fig. 1.** A thermal ellipsoid plot of the title compound illustrating the crystallographic numbering scheme. Thermal ellipsoids are shown at 40% probability.

**Table 2.** Atomic Coordinates ($10^4$) and Equivalent Isotropic Thermal Parameters ($10^2$)

| Atom | *x* | *y* | *z* | $U_{eq}$[a] |
|---|---|---|---|---|
| S | 1855(1) | 445(1) | 7630(1) | 36(1) |
| C(1) | 493(1) | −2684(2) | 5830(2) | 32(1) |
| C(2) | −320(1) | −2687(2) | 4990(2) | 31(1) |
| C(3) | 684(1) | −3949(2) | 4094(2) | 31(1) |
| C(4) | 799(1) | −1215(2) | 6130(2) | 34(1) |
| C(5) | 1529(1) | −1225(2) | 7121(2) | 37(1) |
| N(1) | −154(1) | −3460(2) | 4013(2) | 33(1) |
| N(2) | 1069(1) | −3490(2) | 5138(2) | 34(1) |
| N(3) | 2354(1) | 1171(2) | 6604(2) | 43(1) |
| O(1) | −987(1) | −2114(2) | 5172(1) | 46(1) |
| O(2) | 980(1) | −4674(2) | 3321(1) | 44(1) |
| O(3) | 2462(1) | 231(2) | 8655(1) | 54(1) |
| O(4) | 1107(1) | 1250(2) | 7788(2) | 53(1) |

[a] Equivalent isotropic $U$ defined as one third the trace of the orthogonalized $U_{ij}$ tensor.

were recorded on a Bruker DPX-300 MHz with $d_6$-DMSO as solvent. FAB mass spectra were obtained in a matrix of glycerol with a Fisons ProSpec triple sector mass spectrometer equipped with an LSIMS 40 KV cesium primary gun.

IR(microns): 3.05 $\mu$, broad, NH of hydantoin and sulfonamide; 5.65 $\mu$, CO of hydantoin; 5.76 $\mu$, 5.84 $\mu$, broad, urea CO of hydantoin; 6.48 $\mu$, NH of $SO_2NH_2$; 7.55 $\mu$, 8.77 $\mu$, S → O of $SO_2NH_2$.

$^1$H NMR: $\delta$ 10.6 (s, 1H, imide N*H* of hydantoin); 8.05 (s, 1H, amide N*H* of hydantoin); 6.91 (s, 2H, $NH_2$ of $-SO_2NH_2$); 4.17 (m, 1H, $-CH-CH_2-$); 3.07 (m, 2H, $-CH_2-SO_2NH_2$); 2.10 (m, 1H, $-CH_2-CH_2-SO_2NH_2$); 1.90 (m, 1H, $-CH_2-CH_2-SO_2NH_2$).

$^{13}$C NMR: $\delta$ 175.4 (*C*O); 157.3 (urea *C*O of hydantoin); 56.1 ($-CH-CH_2-$); 50.5 ($-CH_2-SO_2NH_2$); 26.6 ($-CH_2-CH_2-SO_2NH_2$).

FAB-MS: molecular ion peak $MH^+$ at 208.

### *Single-crystal analysis*

X-ray measurements were carried out on an Enraf-Nonius CAD4 automated diffractometer using Mo K$\alpha$ radiation ($\lambda = 0.71073$ Å). Intensity data were corrected for Lorentz and polarization effects after which a semiempirical absorption correction was applied. The structure was solved using SHELXTL-PC[7] and refined against all $F^2$ data using SHELXL-97.[8] All non-hydrogen atoms were assigned anisotropic displacement parameters. The hydrogen atoms involved in the hydrogen bonding network (except H5b) were located in difference Fourier syntheses; their positional parameters were refined with fixed isotropic thermal parameters [$U_{iso}$(H) = 1.2 × $U_{iso}$(parent)]. The remaining protons were included in calculated positions and allowed to ride on their parent carbon atoms with fixed isotropic thermal parameters [$U_{iso}$(H) = 1.2 × $U_{iso}$(C)]. A summary of experimental data is presented in Table 1.

**Table 3.** Selected Geometric Parameters for **1** in (Å) and (°)

| | | | | | |
|---|---|---|---|---|---|
| S−O(4) | 1.428(2) | S−O(3) | 1.436(2) | S−N(3) | 1.591(2) |
| S−C(5) | 1.769(2) | C(1)−N(2) | 1.455(3) | C(1)−C(2) | 1.514(3) |
| C(1)−C(4) | 1.524(3) | C(2)−O(1) | 1.212(2) | C(2)−N(1) | 1.356(3) |
| C(3)−O(2) | 1.224(2) | C(3)−N(2) | 1.335(3) | C(3)−N(1) | 1.390(2) |
| C(4)−C(5) | 1.518(3) | | | | |
| O(4)−S−O(3) | 118.57(10) | O(4)−S−N(3) | 107.60(11) | O(3)−S−N(3) | 107.21(10) |
| O(4)−S−C(5) | 108.48(10) | O(3)−S−C(5) | 106.02(10) | N(3)−S−C(5) | 108.65(10) |
| N(2)−C(1)−C(2) | 101.6(2) | N(2)−C(1)−C(4) | 114.5(2) | C(2)−C(1)−C(4) | 111.7(2) |
| O(1)−C(2)−N(1) | 127.4(2) | O(1)−C(2)−C(1) | 126.1(2) | N(1)−C(2)−C(1) | 106.5(2) |
| O(2)−C(3)−N(2) | 128.6(2) | O(2)−C(3)−N(1) | 123.9(2) | N(2)−C(3)−N(1) | 107.5(2) |
| C(5)−C(4)−C(1) | 110.9(2) | C(4)−C(5)−S | 113.9(2) | C(2)−N(1)−C(3) | 112.2(2) |
| C(3)−N(2)−C(1) | 112.2(2) | | | | |
| N(2)−C(1)−C(4)−C(5) | −74.1(2) | C(1)−C(4)−C(5)−S | −174.2(1) | C(4)−C(5)−S−N(3) | −72.5(2) |
| C(4)−C(5)−S−O(3) | 172.8(2) | C(4)−C(5)−S−O(4) | 44.4(2) | | |

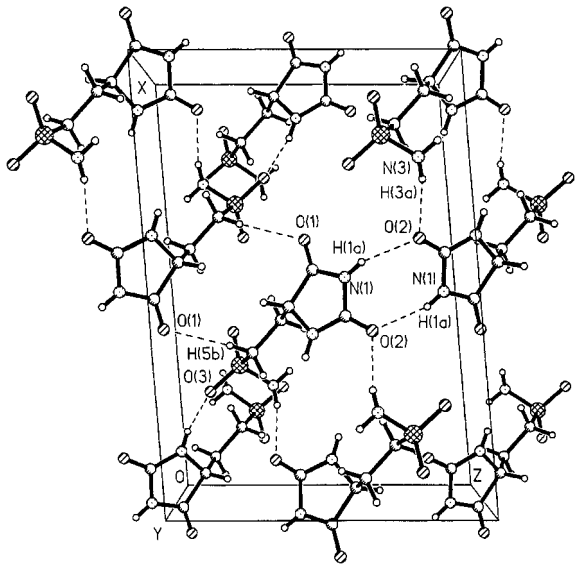


**Fig. 2.** A representation of the molecular packing arrangement in the unit cell illustrating the network of intermolecular interactions.

## Results and discussion

The crystallographic data of **1** best fit a monoclinic lattice, space group *C*2/*c* (No. 15). The molecular structure is illustrated in Fig. 1. Atomic coordinates are tabulated in Table 2 while select geometric parameters are presented in Table 3.

The title compound contains a hydantoin ring attached to an ethylsulfonamide chain at the chiral center [C(1)] of the ring (again see Fig. 1). Both enantiomers are observed in the crystal structure, as is required for centrosymmetric space groups. All bond distances are internally consistent and in agreement with experimental values found in similar compounds.[6] Molecules are in an extended structure as shown in Fig. 1 with a C(1)−C(4)−C(5)−S torsion angle of −174.2(1)°. The atoms in the hydantoin (imidazolidinedione) ring are planar as expected[6] with a mean standard deviation of 0.008 Å. Five of the six bond angles of the sulfonamide group are within a few degrees of tetrahedral as listed in Table 3 while the O(4)−S−O(3) was determined to be 118.57(10)° giving the sulfonamide group distorted tetrahedral geometry.

Figure 2 illustrates the molecular packing arrangement in the unit cell. A three-dimensional network of intermolecular hydrogen bonding occurs within the crystal lattice involving all of the N−H and O atoms of the imidazolidinedione ring and the sulfonamide functional group. Intermolecular contact distances are presented in Table 4. According to the somewhat liberal definition ascribed by Desiraju and Steiner,[9] the C(5)−H(5b)···O(1) contact may be described as a weak hydrogen bond.

**Table 4.** Analysis of Potential Hydrogen Bonding in **1**

| Atom | D−H | H···A | D···A | D−H···A |
|---|---|---|---|---|
| N(1)−H(1a)···O(2)[a] | 0.78(2) | 2.30(2) | 3.030(2) | 155(2) |
| N(2)−H(2)···O(3)[b] | 0.85(2) | 2.02(2) | 2.845(2) | 165(2) |
| N(3)−H(3a)···O(2)[c] | 0.81(2) | 2.19(3) | 2.978(3) | 168(2) |
| N(3)−H(3b)···O(1)[d] | 0.84(3) | 2.10(3) | 2.929(3) | 167(2) |
| C(5)−H(5b)···O(1)[e] | 0.97 | 2.38 | 3.292(3) | 156 |

[a] $-x, y, -z + 1/2$.
[b] $-x + 1/2, y - 1/2, -z + 3/2$.
[c] $-x + 1/2, -y - 1/2, -z + 1$.
[d] $-x, -y, -z + 1$.
[e] $-x, y, -z + 3/2$.

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