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## Stereospecific ligands and their complexes. VI. The crystal structure of (S,S)-ethylenediamine-*N,N'*-di-2-propanoic acid hydrochloride, (S,S)-H<sub>2</sub>edd<sup>+</sup>·HCl<sup>⊖</sup>

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**Abstract:** (S,S)-Ethylenediamine-*N,N'*-di-2-propanoic acid hydrochloride, (S,S)-H<sub>2</sub>edd<sup>+</sup>·HCl<sup>⊖</sup>, was prepared and its crystal structure determined. The compound was characterized by infrared and <sup>1</sup>H- and <sup>13</sup>C-NMR spectroscopy. It forms *P*1 in the space group of a triclinic crystal system with *a* = 5.3902(2) Å, *b* = 5.8967(2) Å, *c* = 10.3319(2) Å,  $\alpha$  = 99.625(2)°,  $\beta$  = 91.645(2)°,  $\gamma$  = 109.995(2)° and *Z* = 1.

**Keywords:** (S,S)-ethylenediamine-*N,N'*-di-2-propanoate ligand; X-ray crystal structure, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR spectroscopy.

### INTRODUCTION

The discovery of the anticancer activity of cisplatin led investigators to synthesize a number of platinum(II/IV) complexes that could potentially be less toxic to healthy tissues<sup>1–3</sup> and overcome the resistance of some tumors to this type of drug.<sup>4,5</sup> Although platinum-based drugs have high nephrotoxicity and neurotoxicity, cisplatin, carboplatin and oxaliplatin are in clinical use worldwide.<sup>6</sup>

According to these investigations, attention was mainly focused on the preparation, characterization and biological activity of metal complexes with stereospecific edda-type ligands (edda = ethylenediamine-*N,N'*-diacetato ion), such as the ethylenediamine-*N,N'*-di-(S,S)-2-propanoate ion and its derivatives.<sup>7–10</sup>

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The preparation of (*S,S*)-ethylenediamine-*N,N'*-di-2-propanoic acid was published earlier, without spectral characterization.<sup>11</sup> In the present study, the ligand was characterized by infrared, and <sup>1</sup>H- and <sup>13</sup>C-NMR spectroscopy. In addition, this paper reports single crystal X-ray structure determination of (*S,S*)-ethylenediamine-*N,N'*-di-2-propanoic acid hydrochloride, crystallized from an HCl–water solution (pH 1.0).

## EXPERIMENTAL

### Chemistry

All reagents were of grade purity. (*S,S*)-Ethylenediamine-*N,N'*-di-2-propanoic acid, ((*S,S*)-H<sub>2</sub>eddp), was prepared using a previously described procedure.<sup>11</sup> On leaving an HCl–water solution of (*S,S*)-H<sub>2</sub>eddp (pH 1.0) to stand at room temperature for several days, (*S,S*)-ethylenediamine-*N,N'*-di-2-propanoic acid hydrochloride, (*S,S*)-H<sub>2</sub>eddp·HCl, crystallized in a form suitable for X-ray crystal structure determination.

### Crystal structure determination

A colorless block-shaped single crystal of (*S,S*)-H<sub>2</sub>eddp·HCl was sealed into a glass capillary and used for the measurement of precise cell constants and intensity data collection. The data were collected at room temperature on a Bruker-Nonius KappaCCD using MoK $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ , graphite monochromator). The diffraction intensities were corrected for Lorentz and polarization effects. The absorption effects were corrected on a semi-empirical basis using multiple scans (SADABS).<sup>12</sup> The structure was solved by direct methods and refined by full-matrix least-squares calculations against  $F^2$ .<sup>13</sup> All non-hydrogen atoms were refined with anisotropic displacement parameters. The position of all hydrogen atoms were derived from a different Fourier synthesis and all hydrogen atoms were refined with individual isotropic displacement parameters. The details of the crystal data, data collection and structure refinement are summarized in Table I.

TABLE I. Crystal data, data collection and structure refinement details for (*S,S*)-H<sub>2</sub>eddp·HCl

Formula	C <sub>8</sub> H <sub>17</sub> ClN <sub>2</sub> O <sub>4</sub>
Formula weight	240.69
Crystal system	Triclinic
Space group	P1
<i>a</i> / Å	5.3902(2)
<i>b</i> / Å	5.8967(2)
<i>c</i> / Å	10.3319(2)
$\alpha$ / °	99.625(2)
$\beta$ / °	91.645(2)
$\gamma$ / °	109.995(2)
<i>V</i> / Å <sup>3</sup>	302.94(2)
<i>Z</i>	1
Density (calcd.) $\times 10^{-3}$ , kg m <sup>-3</sup>	1.319
Abs. coefficient, mm <sup>-1</sup>	0.314
<i>F</i> (000)	128
No. of collected reflections	8159
No. of independent reflections	2941 ( <i>R</i> (int) = 0.0277)
No. of observed reflection ( <i>I</i> > 2 $\sigma$ ( <i>I</i> ))	2510



TABLE I. Continued

$T_{\min}$ , $T_{\max}$	0.917, 1.000
Largest difference peak/hole, eÅ <sup>-3</sup>	0.215–0.221
Goof ( $F^2$ )	1.024
$R_1$ , $wR_2$ ( $I > 2\sigma(I)$ )	0.0318, 0.0670
$R_1$ , $wR_2$ (all data)	0.0438, 0.0704
Absolute structure parameter	0.00(4)

The infrared spectrum was recorded on a Perkin-Elmer FTIR 31725-X spectrophotometer using the KBr pellet technique. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded on Varian Gemini-200 NMR spectrometer using TMS in D<sub>2</sub>O as internal reference at 22 °C using a 10 mM solution of the compound. Elemental analyses was realized on a Vario III CHNOS elemental analyzer, Elemental Analysensysteme, GmbH.

All the reagents were obtained commercially and used without further purification.

## RESULTS AND DISCUSSION

### *Spectroscopic properties of (S,S)-H<sub>2</sub>eddp·HCl*

Yield: 11.3 %; Anal. Calcd. for C<sub>8</sub>H<sub>17</sub>ClN<sub>2</sub>O<sub>4</sub>: C, 39.92; H, 7.12; N, 11.64 %. Found: C, 39.70; H, 7.01; N, 11.50 %. IR (KBr, cm<sup>-1</sup>): 3419, 3120, 2828, 1728, 1693, 1456, 1350, 1275, 1118, 922, 837, 790, 626. <sup>1</sup>H-NMR (200 MHz, D<sub>2</sub>O, δ / ppm): 1.53 (6H, d, CH<sub>3</sub>), 3.54 (4H, t, CH<sub>2</sub>), 3.67 (2H, q, CH). <sup>13</sup>C-NMR (200 MHz, D<sub>2</sub>O, δ / ppm): 17.4 (CH<sub>3</sub>), 44.7 (CH<sub>2</sub>), 60.1 (CH), 175.7 (COO<sup>-</sup>).

The IR spectrum of the ligand showed specific absorption bands, *i.e.*, δ(C=O) at 1728 cm<sup>-1</sup> (strong), typical absorption for a protonated acid, δ(C=O) at 1693 cm<sup>-1</sup> (strong), typical absorption for a deprotonated acid, δ(C–O) 1275 cm<sup>-1</sup> (medium) and δ(CH<sub>3</sub>) at 2828 cm<sup>-1</sup> (medium).

The NMR spectroscopic measurements gave proof for the constitution of the ligand. In the <sup>1</sup>H-NMR spectrum of (S,S)-H<sub>2</sub>eddp·HCl, there are the expected signals of CH<sub>2</sub> protons between two diamine nitrogen atoms at 3.54 ppm as a triplet. The signal for the hydrogen atoms of the methyl groups is located at 1.53 ppm as a doublet. The signal for the hydrogen atoms of the CH groups is at 3.67 ppm as a quartet.

<sup>13</sup>C-NMR spectrum of (S,S)-H<sub>2</sub>eddp·HCl exhibits signals for the carbon atom of the COOH groups at 175.7 ppm. The signal of the carbon atom of the methyl groups is at 17.4 ppm. The carbon atoms of the CH<sub>2</sub> groups gave a signal at 44.7 ppm and of the CH groups a signal at 60.1 ppm.

### *Description of the structure of (S,S)-H<sub>2</sub>eddp·HCl*

Using the previously described procedure,<sup>11</sup> (S,S)-ethylenediamine-*N,N'*-di-2-propanoic acid, (S,S)-H<sub>2</sub>eddp, was isolated as a double zwitter ion at pH 5, with two secondary nitrogen atoms and two carboxylic groups in its structure (Fig. 1). Acidification with aqueous HCl solution to pH 1 resulted in the proto-



nation of one carboxylic group of the (*S,S*)-H<sub>2</sub>eddp molecule. This protonated hydrochloride form of (*S,S*)-H<sub>2</sub>eddp yielded good quality crystals suitable for X-ray structure determination.

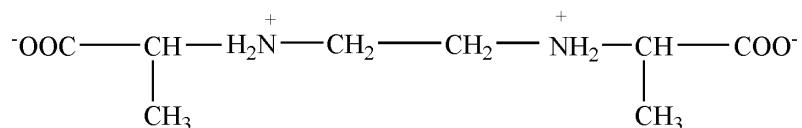


Fig. 1. Structure of (*S,S*)-H<sub>2</sub>eddp as a zwitter ion.

The molecular structure of (*S,S*)-H<sub>2</sub>eddp·HCl with the corresponding atomic numbering scheme is shown in Fig. 2. The unit cell packing of the (*S,S*)-H<sub>2</sub>eddp·HCl molecule is given in Fig. 3, while selected bond distances and bond angles are listed in Table II.

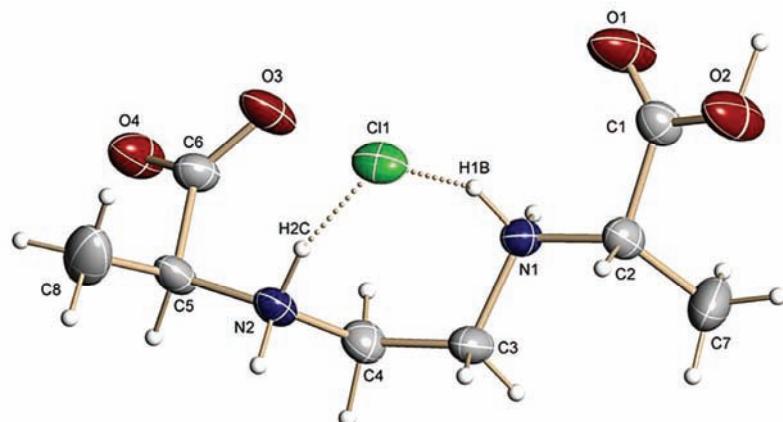


Fig. 2. Molecular structure of (*S,S*)-H<sub>2</sub>eddp·HCl (50 % probability ellipsoids, H atoms displayed at arbitrary size), the dotted lines indicate the hydrogen bonds between the chloride anion and the (*S,S*)-eddp cation.

The structure of (*S,S*)-H<sub>2</sub>eddp·HCl consists of the protonated (*S,S*)-H<sub>2</sub>eddp·HCl molecule, as a (*S,S*)-H<sub>3</sub>eddp<sup>+</sup> and a Cl<sup>-</sup> counter ion. The difference between the O(1)–C(1) and O(2)–C(1) bond lengths (Table II) suggest the protonation of this carboxylic group, while the O(3)–C(6) and O(4)–C(6) bonds were of almost the same length, suggesting the deprotonated form of this carboxylic group. The elongation of the N(2)–H(2C) bond compared to the N(2)–H(2B) bond is due to the fact that H(2C) is incorporated in a hydrogen bond with Cl<sup>-</sup> (Table III). All the other bond distances and angles are in their usual ranges.

The specific shape of the central diamine part of the (*S,S*)-H<sub>2</sub>eddp·HCl molecule is a consequence of the strong intermolecular N(1)–H(1B)…Cl(1) and N(2)–H(2C)…Cl(1) hydrogen bonds. These N–H…Cl hydrogen bonds, strong inter-

molecular N–H···Cl and O–H···O hydrogen bonds as well as weaker C–H···Cl hydrogen bonds (Table III) determine the packing of the (S,S)-H<sub>2</sub>eddp·HCl molecules in the crystal lattice. The parameters of the more unusual and weaker C–H···Cl hydrogen bonding interactions fall within the typical range observed for this type of hydrogen bond.<sup>14</sup>

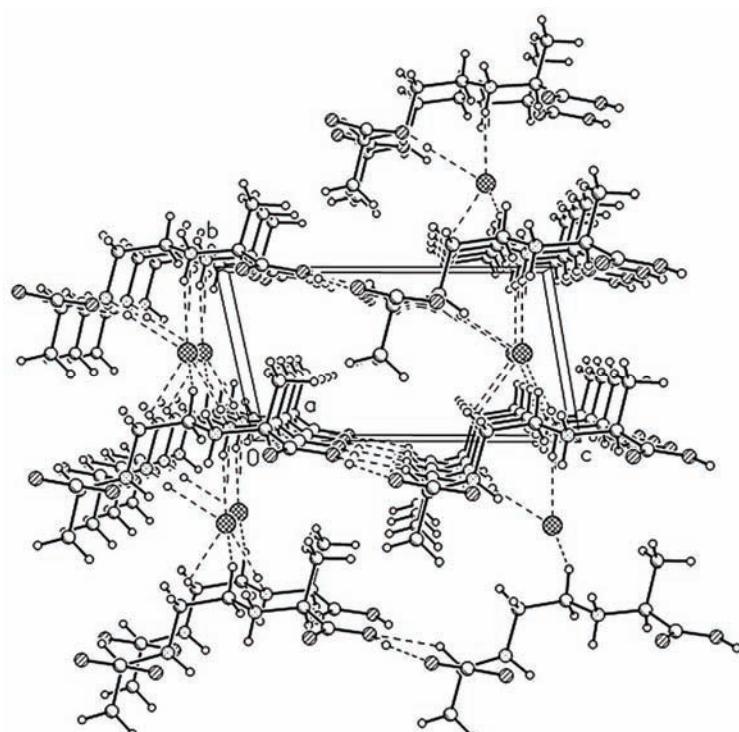


Fig. 3. Packing diagram of (S,S)-H<sub>2</sub>eddp·HCl (view along the crystallographic *a*-axis); dotted lines indicate intramolecular hydrogen bonds.

TABLE II. Selected bond distances and angles for (S,S)-H<sub>2</sub>eddp·HCl (estimated standard deviations (e.s.d.'s) in parentheses)

Bond	Distance, Å	Value
O(1)–C(1)		1.196(2)
O(2)–C(1)		1.292(2)
O(3)–C(6)		1.244(2)
O(4)–C(6)		1.255(2)
N(1)–C(3)		1.491(2)
N(1)–C(2)		1.493(2)
N(2)–C(5)		1.494(2)
N(2)–C(4)		1.495(2)
C(1)–C(2)		1.519(3)

TABLE II. Continued

Bond	Value
	Distance, Å
C(2)–C(7)	1.527(3)
C(3)–C(4)	1.510(3)
C(5)–C(8)	1.511(3)
C(5)–C(6)	1.540(2)
N(1)–H(1A)	0.930(3)
N(1)–H(1B)	0.930(2)
N(2)–H(2B)	0.94(3)
N(2)–H(2C)	0.98(3)
	Angle, °
C(5)–N(2)–C(4)	113.72(15)
O(1)–C(1)–O(2)	126.11(18)
O(1)–C(1)–C(2)	122.76(16)
O(2)–C(1)–C(2)	111.13(15)
N(1)–C(2)–C(1)	107.63(13)
N(1)–C(2)–C(7)	111.68(17)
C(1)–C(2)–C(7)	111.28(17)
N(1)–C(3)–C(4)	112.56(15)
N(2)–C(4)–C(3)	112.39(16)
N(2)–C(5)–C(8)	108.85(17)
N(2)–C(5)–C(6)	109.53(14)
C(8)–C(5)–C(6)	109.89(18)
O(3)–C(6)–O(4)	125.48(16)
O(3)–C(6)–C(5)	117.41(16)
O(4)–C(6)–C(5)	117.04(15)
C(3)–N(1)–C(2)	113.01(13)

TABLE III. Hydrogen bonds found for (*S,S*)-H<sub>2</sub>eddp·HCl (e.s.d.'s in parentheses); Symmetry transformations used to generate equivalent atoms: #1:  $x, y+1, z$ ; #2:  $x+1, y, z$ ; #3:  $x, y, z+1$ ; #4:  $x+1, y+1, z$ 

D–H···A	$d(D–H) / \text{\AA}$	$d(H\cdots A) / \text{\AA}$	$d(D\cdots A) / \text{\AA}$	$\angle(DHA) / {}^\circ$
N(1)–H(1A)···Cl(1)#1	0.93(3)	2.25(3)	3.1254(15)	158(2)
N(1)–H(1B)···Cl(1)	0.93(2)	2.32(2)	3.0866(15)	138.8(17)
N(2)–H(2B)···O(3)#2	0.94(2)	1.80(2)	2.7239(19)	167(2)
N(2)–H(2C)···Cl(1)	0.98(3)	2.22(3)	3.1659(16)	160(2)
O(2)–H(2D)···O(4)#3	0.97(4)	1.61(4)	2.523(2)	153(4)
C(3)–H(3B)···Cl(1)#4	0.96(3)	2.62(2)	3.321(2)	130(2)
C(4)–H(4B)···Cl(1)#1	0.98(2)	2.88(2)	3.591(2)	130(2)

## CONCLUSIONS

(*S,S*)-Ethylenediamine-*N,N'*-di-2-propanoic acid was unexpectedly crystallized in the form of the monohydrochloride. The crystal form and the crystal packing are determined by strong intermolecular N(1)–H(1B)···Cl(1) and N(2)–H(2C)···Cl(1), as well as by unusually weak C(3)–H(3B)···Cl(1)#4 and C(4)–



$\text{--H(4B)} \cdots \text{Cl(1)\#1}$  hydrogen bonds. The bond distances and bond angles are within their usual ranges.

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*Supplementary data.* Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication No. CCDC-795801. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: int. code +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk).

#### И З В О Д

СТЕРЕОСПЕЦИФИЧНИ ЛИГАНДИ И ЊИХОВИ КОМПЛЕКСИ. VI. КРИСТАЛНА СТРУКТУРА (*S,S*)-ЕТИЛЕНДИАМИН-*N,N'*-ДИ-2-ПРОПАНСКА КИСЕЛИНА-ХИДРОХЛОРИДА, (*S,S*)-H<sub>2</sub>eddp-HCl

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Синтетисан је тетрадентатни лиганд (*S,S*)-етилендиамин-*N,N'*-ди-2-пропанска киселина-хидрохлорид и испитивана је његова кристална структура. Наведени лиганд неочекивано кристалише као монохидрохлорид у просторној групи Р1 триклиничног кристалног система са димензијама јединичне ћелије  $a = 5,3902(2)$  Å,  $b = 5,8967(2)$  Å,  $c = 10,3319(2)$  Å,  $\alpha = 99,625(2)^\circ$ ,  $\beta = 91,645(2)^\circ$ ,  $\gamma = 109,995(2)^\circ$  и  $Z = 1$ .

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