

## Walden Inversion

### III. The Crystal Structure and Absolute Configuration of Zn(II) (+)-Aspartate Trihydrate

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L-(+)-Aspartic acid can be converted into, e.g., (-)-malic acid and (-)-chlorosuccinic acid according to the choice of reagents. These facts were used by Walden<sup>1</sup> for his discovery of the sequence of reactions called the Walden cycle. The structures and absolute configurations of (-)-chlorosuccinic acid and of (-)-malic acid have been determined recently<sup>2,3</sup> and we considered it desirable also to determine the absolute configuration of aspartic acid. Doyne, Pepinsky and Watanabe<sup>4</sup> reported cell dimensions of salts of L-aspartic acid with divalent zinc, cobalt, and nickel. They report that the salts crystallize as trihydrates and that they are isomorphous. They determined the structure and abso-

lute configuration of the cobaltous salt and used the coordinates from this to refine the structural parameters of the zinc salt.

The report by Doyne *et al.*<sup>4</sup> is without details; no coordinates are listed. We aimed at a repetition of their work in order to check our results against theirs.

*Experimental.* We were unable to obtain crystals of cobalt (II) and nickel (II)-aspartate. We made several attempts using the prescriptions of Lifschitz and Schouteden<sup>5</sup> and several variants of their methods. Zinc(II)-aspartate, however, yielded crystals readily. The aspartic acid was a Fluka *puriss.* product of specific optical rotation  $[\alpha]_D^{25.5} = +3.2^\circ/\text{cm}$  (1 % solution in 6 M HCl). Three-dimensional intensity data were collected using a linear diffractometer of Arndt-Phillips design. All reflections within a hemisphere of reciprocal space were recorded out to a Bragg angle of  $27^\circ$ . MoK $\alpha$ -radiation was selected by a graphite monochromator. The reflections which were recorded near the spindle axis of the linear diffractometer were remeasured using a four-circle Picker diffractometer. A set of non pinacoid Friedel related intensities  $|F(hkl)|^2$  and  $|F(\bar{h}\bar{k}\bar{l})|^2$  were measured using the Picker diffractometer and WL $\beta_1$ -radiation.

Crystal data are as follows: ZnC<sub>4</sub>H<sub>5</sub>O<sub>4</sub>N. 3H<sub>2</sub>O,  $a = 9.443(5)$ ,  $b = 7.862(4)$ ,  $c = 11.696(6)$

Table 1. Fraction 1 coordinates  $\times 10^4$  and thermal parameters,  $U_{ij}$  ( $\text{Å}^2$ )  $\times 10^4$ , as they appear in the temperature factor expression:  $\exp(-2\pi^2 a_i^2 a_j^2 h_i h_j U_{ij})$ . Estimated standard deviations in the last significant figures are in parentheses.

	x/a	y/b	z/c	U <sub>11</sub>	U <sub>22</sub>	U <sub>33</sub>	U <sub>12</sub>	U <sub>13</sub>	U <sub>23</sub>
Zn	452 ( 3)	1359 ( 3)	923 ( 2)	1453 ( 12)	1585 ( 12)	2161 ( 11)	91 ( 12)	-115 ( 12)	110 ( 12)
O(1)	1510 (24)	2532 (27)	2416 (16)	2565 (104)	2120 ( 96)	3440 ( 91)	648 ( 87)	-692 ( 86)	-582 ( 82)
O(2)	3477 (25)	2075 (30)	3451 (18)	3113 (116)	3420 (120)	3881 ( 98)	357 (105)	-1473 (101)	-932 ( 96)
O(3)	2448 (21)	1800 (27)	33 (16)	1590 ( 90)	2588 (108)	2872 ( 82)	148 ( 79)	205 ( 73)	850 ( 78)
O(4)	4705 (20)	1278 (26)	-458 (17)	2026 ( 94)	1947 ( 94)	3900 ( 90)	308 ( 93)	1044 ( 80)	601 ( 83)
N	1348 (27)	-736 (32)	1729 (19)	2079 (107)	1679 (109)	2694 ( 95)	-227 ( 97)	117 ( 93)	213 ( 90)
C(1)	2560 (30)	1635 (36)	2728 (21)	2197 (125)	2067 (138)	2088 ( 93)	57 (107)	-54 ( 98)	-106 ( 99)
C(2)	2734 (29)	-154 (36)	2179 (20)	2028 (128)	1635 (120)	2128 ( 98)	144 (104)	-331 ( 97)	367 (104)
C(3)	3868 (31)	-107 (40)	1227 (21)	2042 (138)	2200 (140)	2769 (116)	467 (117)	186 (100)	378 (104)
C(4)	3623 (28)	1088 (33)	206 (20)	1754 (114)	1337 (126)	2542 (100)	-33 (101)	212 ( 95)	-59 ( 95)
O(W1)	-310 (25)	263 (31)	-601 (18)	2027 (110)	3899 (123)	3281 ( 94)	44 (102)	97 ( 82)	-1085 ( 89)
O(W2)	-1572 (26)	946 (35)	1763 (20)	2626 (115)	2510 (130)	3145 (101)	-299 ( 97)	217 ( 90)	-41 ( 92)
O(W3)	1992 (26)	6041 (32)	385 (20)	2746 (115)	2656 (126)	3711 (110)	-261 ( 98)	-20 ( 92)	247 ( 99)
	x/a	y/b	z/c	U	x/a	y/b	z/c	U	
CH(2)	3084 (431)	-1144 (542)	2703 (329)	54 (12)	H2(W2)	-2198 (565)	1209 (710)	1240 (476)	71 (14)
CH(31)	4745 (348)	239 (435)	1555 (258)	23 ( 8)	H1(W3)	1393 (529)	5329 (681)	523 (379)	45 (14)
CH(32)	4144 (472)	-1268 (563)	868 (322)	50 (13)	H2(W3)	1976 (517)	6490 (617)	-137 (409)	52 (14)
H1(W1)	285 (517)	-506 (668)	-935 (356)	56 (13)	NH(1)	771 (328)	-1031 (433)	2329 (257)	25 ( 8)
H2(W1)	-1146 (416)	-147 (491)	-632 (282)	39 ( 9)	NH(2)	1451 (521)	-1721 (614)	1285 (379)	45 (13)
H1(W2)	-1758 (616)	240 (770)	1946 (431)	65 (20)					

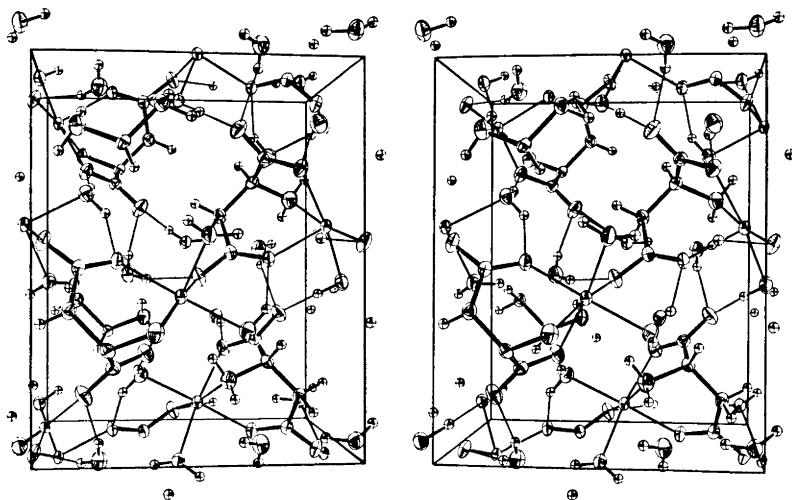


Fig. 1. Perspective drawing of the content of a unit cell of zinc(II) aspartate trihydrate

$\text{\AA}$ .  $V_c = 686.3 \text{ \AA}^3$ , density (calc) 1.92, exp.<sup>4</sup> 1.97  $\text{gem}^{-3}$ ,  $Z = 4$ , space group  $P2_12_12_1$  (No. 19 Int. Tables). Systematic absences  $h00$  for  $h = \text{odd}$ ,  $0k0$  for  $k = \text{odd}$ , and  $00l$  for  $l = \text{odd}$ .

The structure was redetermined without using the preliminary data of Doyne *et al.* by direct methods employing the program system SYMBAD.<sup>6</sup> The first electron density map revealed the positions of all non-hydrogen atoms. By successive applications of least squares refinement and difference electron density maps the positions of the hydrogen atoms were determined also. The parameters from the least squares computations are given in Table 1. The structure was refined to a conventional  $R$ -value of 2.5% using 1279 reflections considered to be of observable magnitude.\* The crystal was regularly and almost centro symmetrically shaped with a radius less than 0.1 mm. No absorption correction was introduced, as  $\exp(-\mu t)$  varies 2% in the angular range of measurements. The linear absorption coefficient for  $\text{MoK}\alpha$  is  $29.4 \text{ cm}^{-1}$ . An isotropic extinction factor  $g$  was refined to a value of 213(14) (dimensionless), thus yielding extinction corrections to  $F_c^2$  ranging from 0.65 to 1.00. This extinction factor corresponds to a mean domain size of 151  $\text{\AA}$  or a mosaic spread of 273 sec. A projection of the structure is shown in Fig. 1. Bond lengths are shown in Table 2.

\* A structure factor table can be obtained from the authors at request.

Table 2. Interatomic distances in  $\text{\AA}$  units. Estimated standard deviations in the last significant figures are in parentheses.

Bond lengths $\text{\AA}$			Bond lengths $\text{\AA}$		
O(1) - C(1)	1.270	(4)	Zn - N	2.077	(2)
O(2) - C(1)	1.259	(3)	Zn - O(5 <sup>1</sup> )	2.106	(2)
C(1) - C(2)	1.554	(4)	Zn - O(2 <sup>2</sup> )	2.173	(3)
C(2) - N	1.482	(4)	O(3 <sup>1</sup> ) - H1(3 <sup>1</sup> )	0.913	(51)
C(2) - CH(2)	1.044	(41)	O(4 <sup>1</sup> ) - H2(4 <sup>1</sup> )	0.853	(39)
C(2) - C(3)	1.545	(4)	O(2 <sup>2</sup> ) - H1(2 <sup>2</sup> )	0.623	(58)
C(3) - CH(31)	0.952	(33)	O(2 <sup>2</sup> ) - H2(2 <sup>2</sup> )	0.875	(58)
C(3) - CH(32)	1.038	(44)	O(4 <sup>2</sup> ) - H1(4 <sup>2</sup> )	0.812	(53)
C(3) - C(4)	1.536	(4)	O(4 <sup>2</sup> ) - H2(4 <sup>2</sup> )	0.706	(50)
C(4) - O(3)	1.258	(3)	O(3 <sup>3</sup> ) - O(2)	2.739	(3)
C(4) - O(4)	1.292	(3)	O(3 <sup>3</sup> ) - O(2)	2.756	(3)
N - NH(1)	0.917	(32)	O(1 <sup>1</sup> ) - O(4)	2.757	(3)
N - NH(2)	0.938	(47)	O(1 <sup>1</sup> ) - O(3)	2.827	(3)
Zn - O(1)	2.212	(2)	O(2 <sup>2</sup> ) - O(1)	2.850	(4)
Zn - O(3)	2.180	(2)	O(2 <sup>2</sup> ) - O(3)	2.899	(3)
Zn - O(4)	2.060	(2)	O(2 <sup>2</sup> ) - O(4)	2.923	(3)
			O(1 <sup>1</sup> ) - O(4)	2.988	(3)

The absolute configuration was found by computing the ratio  $q_c = F_c^2(hkl)/F_c^2(\bar{h}\bar{k}\bar{l})$  using the  $WL\beta_1$  wave length 1.2818  $\text{\AA}$  ( $\Delta f' = -6.82$ ,  $\Delta f'' = 4.21$  for the zinc atom) and comparing it with the ratio between observed data  $q_o = F_{\text{obs}}^2(hkl)/F_{\text{obs}}^2(\bar{h}\bar{k}\bar{l})$ .

The arbitrarily selected enantiomorph proved to be the correct one. A selection of observed and calculated  $q$ -ratios are shown in Table 3.

The computer programs employed in addition to SYMBAD were data reduction, G4,<sup>7</sup> Fourier Synthesis, FORDAP,<sup>8</sup> least squares refinement, LINUS,<sup>9</sup> plot program, ORTEP,<sup>10</sup> distance and angle calculations, ORFFE,<sup>11</sup>

Table 3.

Comparison of intensities used in the determination of absolute configuration.

The ratio  $q = I(hkl)/I(\bar{h}\bar{k}\bar{l})$  is given as observed with standard deviations  $\times 100$  in parentheses and as calculated. All together 49  $q$ -ratios were measured. None of those left out was in contradiction to the results listed.

hkl	q(obs)	q(calc)	hkl	q(obs)	q(calc)
111	0.77 (1)	0.72	231	1.11 (3)	1.26
113	0.69 (2)	0.69	23 $\bar{1}$	1.14 (2)	1.26
11 $\bar{3}$	0.88 (3)	0.69	234	1.40 (4)	1.66
11 $\bar{5}$	1.47 (6)	1.34	23 $\bar{4}$	1.23 (3)	1.66
123	0.82 (2)	0.91	332	0.90 (3)	0.91
1 $\bar{2}$ 3	0.91 (2)	0.91	332	0.84 (3)	0.91
131	0.61 (1)	0.50	343	0.64 (12)	0.62
1 $\bar{3}$ 1	0.59 (1)	0.50	343	0.71 (14)	0.62
141	1.16 (5)	1.10	361	1.38 (6)	1.42
1 $\bar{4}$ 1	1.15 (5)	1.10	36 $\bar{1}$	1.26 (6)	1.42
211	0.81 (1)	0.72	415	0.58 (2)	0.69
223	0.57 (1)	0.48	324	0.76 (2)	0.72
2 $\bar{2}$ 3	0.65 (1)	0.48	3 $\bar{2}$ 4	0.87 (3)	0.72

L-(+)-Aspartic acid has the *S*-configuration according to the Cahn-Ingold notation. As (-)-chlorosuccinic acid<sup>2</sup> and (-)-malic acid<sup>3</sup> also have the *S*-configuration, no inversion takes place in the reactions leading from aspartic acid to these two compounds. The structural results are in accordance with those of Doyne *et al.*<sup>4</sup> When our structural work was completed, we became aware of a subsequent refinement of the data reported in Ref. 4. Doyne reports refined parameters for Zn(II)-aspartate trihydrate in *Advan. Protein Chem.*<sup>12</sup> These data are probably less accurate than those reported here, but on the average there is a good agreement between the two sets of results.

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## The Effect of Oxygen Lone Pairs on $^1J(^{13}\text{CH})$ Values in 1,3-Dioxanes

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Recently we have shown that  $^1J(^{13}\text{CH})$  values can be used to determine the anomeric configuration in carbohydrate derivatives since the carbon-hydrogen coupling constant is *ca.* 10 Hz larger when the proton is equatorially oriented than when it is axial.<sup>1,2</sup>

We have now studied a number of 1,3-dioxane derivatives and have found that the  $^1J(^{13}\text{CH})$  values are dependent on the orientation of the protons relative to the ring oxygens.

The assignments of the  $^{13}\text{C}$ -chemical shifts are based mainly on published values as shown in Table 1. Undecoupled spectra were obtained using gated decoupling technique.<sup>3</sup>

The  $^1J(^{13}\text{C}-\text{H}_2)$  value of *trans*-2-methyl-5-*t*-butyl-1,3-dioxane (2), or of the corresponding 2-phenyl derivative (3), was 158

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