

Cl atom and the next aromatic group along the stack causes the molecules to pack as discussed above and, in the process, brings about the oxygen–methylene hydrogen contact noted previously. The weakening of the interaction between the *p* substituent and the adjacent phenyl ring in the ditosylate monomer [crude atom–atom potential calculations using the parameters of Bates & Busing (1974) show the contribution of this type of interaction to the lattice energy to be significantly less in the ditosylate] allows the molecules to stack in a form which is translationally slipped relative to the *p*-chloro compound, thereby reducing the oxygen–methylene hydrogen interactions and generally allowing the diacetylenic groups to pack slightly closer. Most importantly, the translation reduces γ_1 to $\sim 45^\circ$ and brings the two potentially reactive carbon atoms into proximity, thereby allowing facile polymerization. Thus the introduction of the chlorine atom is found to cause a profound change in solid-state reactivity *via* a rather subtle alteration of the intrastack packing.

References

- BATES, J. B. & BUSING, W. R. (1974). *J. Chem. Phys.* **60**, 2414–2419.
 BAUGHMAN, R. H. (1974). *J. Polym. Sci.* **12**, 1511–1535.
 DUNITZ, J. D. & ROBERTSON, J. M. (1947). *J. Chem. Soc.* pp. 1145–1156.
 GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.
 HÄDICKE, E., PENZIEN, K. & SCHNELL, H. W. (1974). *Angew. Chem. Int. Ed. Engl.* **10**, 940–941.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.
 KOBELT, D. & PAULUS, E. F. (1973). *Acta Cryst.* **B30**, 232–234.
 MAYERLE, J. J. (1977). *Inorg. Chem.* **16**, 916–919.
 SCHMIDT, G. M. J. (1971). *Pure Appl. Chem.* **27**, 647–678.
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
 WEGNER, G. (1969). *Z. Naturforsch. Teil B*, **246**, 824–832.
 WEGNER, G. (1971). *Makromol. Chem.* **145**, 85–94.
 WIEBENGA, E. H. (1940). *Z. Kristallogr.* **102**, 193–206.

Acta Cryst. (1978). **B34**, 147–151

The Crystal Structure and Absolute Configuration of (–)-2-*exo*-Aminobicyclo[3.2.1]octane-2-carboxylic Acid Monohydrate*

BY K. K. CHACKO AND S. K. BHATTACHARJEE

Department of Physics (Crystallography and Biophysics), University of Madras, Guindy Campus, Madras 600025, India

AND R. ZAND AND R. WATER

Biophysics Research Division, University of Michigan, Ann Arbor, Michigan 48105, USA

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$C_9H_{15}NO_2 \cdot H_2O$ is monoclinic, space group $P2_1$, with $a = 12.590$ (13), $b = 6.477$ (8), $c = 5.810$ (7) Å, $\beta = 100.68$ (31)°, $Z = 2$. The structure was refined to an R of 0.051 for 851 counter reflections. The absolute configuration was determined by the Bijvoet method and corresponds to the (1*R*,2*R*,5*S*) configuration. The asymmetric substitution of the amino and carboxyl groups at C(2) significantly affects the mirror symmetry of the bicyclo[3.2.1]octane system.

Introduction

In the course of studies on the effect of cyclic and bicyclic amino acid analogues on the free amino acid pool of rat brain (Zand, Sellinger, Water & Harris, 1974) and on cerebellar protein synthesis (Zand & Water, 1977) it was found that 2-aminobicyclo[3.2.1]-

octane-2-carboxylic acid (hereafter 2-ABO) inhibited a cell-free neuronal homogenate protein synthesizing system. In order to compare the dimensions and stereochemistry of the analogue with the amino acids that were in competition with each other during protein synthesis, it was important to determine the structure of the analogue and its absolute configuration. In protein synthesis, the amino acid must be recognized by the amino acylsynthetase and the amino acid synthetase complex must in turn be recognized by the appropriate tRNA. For this analogue, recognition and activation

* Contribution No. 459 from the Department of Physics (Crystallography and Biophysics), University of Madras, Madras 600025, India.

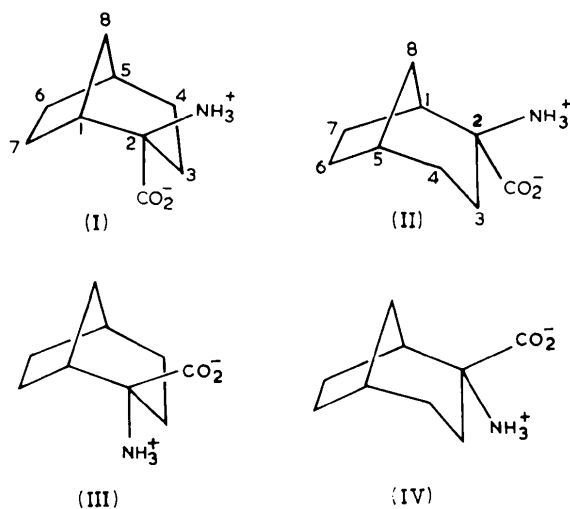


Fig. 1. The four isomers of 2-ABO.

does occur but transfer to the appropriate tRNA does not. However, only the (-) isomers of the *endo* and *exo* forms are active as inhibitors. Thus the X-ray structure determination was necessary to determine which of these structures is 2-amino-*endo* and which is 2-amino-*exo* as well as to determine the absolute configuration of one of the (-) isomers. Fig. 1 shows the four isomers of 2-ABO. (I) and (II) are enantiomorphs having the configuration 2-amino-*exo*, while (III) and (IV) are enantiomorphs having the configuration 2-amino-*endo*, with respect to the bicyclo[3.2.1]octane system.

Experimental

Small, flat plates were grown from water. A crystal 0.1 × 0.3 × 0.3 mm was mounted in a Lindemann-glass tube on a Picker FACS-1 diffractometer such that **b** coincided with the φ axis of the diffractometer. Cell dimensions were determined by a least-squares fit to the settings of 20 reflections.

Crystal data

$C_9H_{17}NO_3$, FW 187.2, $F(000) = 204$, monoclinic, $P2_1$, $Z = 2$, $a = 12.590$ (13), $b = 6.477$ (8), $c = 5.810$ (7) Å, $\beta = 100.68$ (31)°, $D_c = 1.335$ g cm⁻³, $\mu = 6.2$ cm⁻¹, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å.

Intensities of unique reflections with $2\theta \leq 130^\circ$ were measured on a Picker diffractometer. The θ - 2θ scan technique was employed with a 2° min⁻¹ scan speed. The scan range was 3° and background was measured on either side of the peak for 10 s. There were 851 observed reflections; those with $I < 2\sigma(I)$ were considered unobserved and excluded. The data were corrected for Lorentz and polarization factors but not for absorption.

Structure determination and refinement

The structure was solved with *MULTAN* (Declercq, Germain, Main & Woolfson, 1973) based on 200 reflections with $E \geq 1.1$. The E map corresponding to the solution with the highest combined figure of merit revealed the positions of all the non-hydrogen atoms ($R = 0.35$). The solution showed that the amino N atom is *exo* to the bicyclooctane system.

Refinement was by full-matrix least squares (Gantzel, Sparks & Trueblood, 1961). The non-hydrogen atoms were initially refined with isotropic temperature factors to an R of 0.12. A difference synthesis then revealed all the H atoms at expected positions. They were included in the structure factors but not refined. Hughes (1941) type weights were used ($1/w^2$, where $w = |F_o|$ for $|F_o| \geq 20.0$ and $w = 20.0$ for

Table 1. The final positional parameters ($\times 10^4$) of the non-hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	2853 (3)	-435 (8)	8082 (5)
C(2)	1836 (2)	-1135 (8)	6346 (5)
C(3)	2104 (3)	-2905 (8)	4815 (6)
C(4)	2914 (3)	-4494 (9)	6060 (7)
C(5)	3848 (3)	-3494 (9)	7747 (7)
C(6)	4418 (3)	-1792 (10)	6579 (7)
C(7)	3771 (3)	210 (9)	6761 (7)
C(8)	3369 (3)	-2277 (9)	9532 (6)
C(9)	1318 (2)	702 (9)	4851 (6)
N	1000 (2)	-1847 (8)	7748 (5)
O(1)	670 (2)	1805 (7)	5726 (4)
O(2)	1576 (2)	995 (0)	2921 (5)
O(W)	943 (3)	-5812 (8)	9820 (5)

Table 2. Positional ($\times 10^3$) and thermal parameters for the H atoms

Bonded to	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)	
H(1)	N	81	-75	877	2.2
H(2)	N	126	-309	877	2.2
H(3)	N	33	-234	665	2.2
H(4)	C(1)	264	77	918	2.0
H(5)	C(3)	136	-373	409	3.0
H(6)	C(3)	243	-226	337	3.0
H(7)	C(4)	251	-556	704	3.1
H(8)	C(4)	325	-538	476	3.1
H(9)	C(5)	442	-467	857	2.9
H(10)	C(6)	524	-164	752	3.0
H(11)	C(6)	442	-217	479	3.0
H(12)	C(7)	429	136	779	3.3
H(13)	C(7)	346	82	507	3.3
H(14)	C(8)	398	-180	1097	3.1
H(15)	C(8)	276	-320	1020	3.1
H(16)	O(W)	85	-612	832	3.8
H(17)	O(W)	117	-700	1093	3.8

$|F_o| < 20.0$). Anisotropic refinement converged at a final R of 0.051.*

Scattering factors were taken from *International Tables for X-ray Crystallography* (1962). Tables 1 and 2 give the final atomic parameters.

Determination of the absolute configuration

The absolute configuration was determined by the Bijvoet method. Theoretical estimates of the Bijvoet ratios $[\Delta I/I = (I_{hkl} - I_{\bar{h}\bar{k}\bar{l}})/0.5(I_{hkl} + I_{\bar{h}\bar{k}\bar{l}})]$ were calculated from the final coordinates given in Tables 1 and 2 with the $\Delta f'$ and $\Delta f''$ values of C, N and O given by Cromer & Liberman (1970). Twenty reflections with calculated ratios >0.02 were selected from the data. Measurements were made by a procedure which compensates for any short-term instability of the instrument: I_{hkl} and then $I_{\bar{h}\bar{k}\bar{l}}$ were measured successively for each reflection four times. A 3° scan range was used and background measured for 30 s on either side of the peak. The most accurate measurement of Bijvoet ratios could be obtained from the intensity difference between I_{hkl} and $I_{\bar{h}\bar{k}\bar{l}}$ which are exact Bijvoet pairs. Our measurements were made only on exact Bijvoet pairs and not on Bijvoet equivalent pairs I_{hkl} and $I_{\bar{h}\bar{k}\bar{l}}$, where absorption effects are likely to hamper the measurements. Table 3 compares the measured and calculated values. Comparison of the signs (except three reflections shown by an asterisk)

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32841 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. Comparison of observed and calculated Bijvoet ratios

hkl	$100[\Delta I/I]_{\text{calc}}$	$100[\Delta I/I]_{\text{obs}}$
040	-3	-2
240	-3	-6
251	-3	-4
351	+3	-2*
022	-2	-7
912	+2	+1
132	-2	-5
442	+2	-2*
152	-3	-7
523	-4	-4
623	+3	+5
233	+2	-3*
043	-2	-3
443	+7	+9
34 $\bar{1}$	-4	-7
35 $\bar{1}$	+3	+6
53 $\bar{2}$	+4	+5
73 $\bar{2}$	+3	+5
224	+5	+8
42 $\bar{4}$	+2	+6

shows that the absolute configuration is the same as that used for the calculated values, and coordinates in Tables 1 and 2 refer to the correct absolute configuration. The absolute configuration corresponds to the (1*R*,2*R*,5*S*) configuration (Cahn, Ingold & Prelog, 1956) and agrees with that predicted on chemical and correlative bases. The absolute configuration is analogous to that found for the homologous isomer (-)-2-*exo*-aminobicyclo[2.2.1]heptane-2-carboxylic acid hydrobromide (hereafter 2-BCH) (Apgar & Ludwig, 1972).

Results and discussion

The bond lengths and angles are given in Fig. 2, which is drawn for the correct absolute configuration. They show the strain in the bicyclo[3.2.1]octane system. As expected, the one-atom bridge-head angle [C(1)–C(8)–C(5)] of 102.2° is significantly smaller than the two-atom bridge-head angles of 104.9° [C(1)–C(7)–C(6)] and 106.0° [C(5)–C(6)–C(7)], which in turn are significantly smaller than the three-atom bridge-head angles of 110.8° [C(1)–C(2)–C(3)], 115.4° [C(2)–C(3)–C(4)] and 112.6° [C(3)–C(4)–C(5)]. The one-atom bridge-head angle (102.2°) and the angles C(8)–C(1)–C(7) (101.6°) and C(8)–C(5)–C(6) (101.9°) have values much less than the tetra-

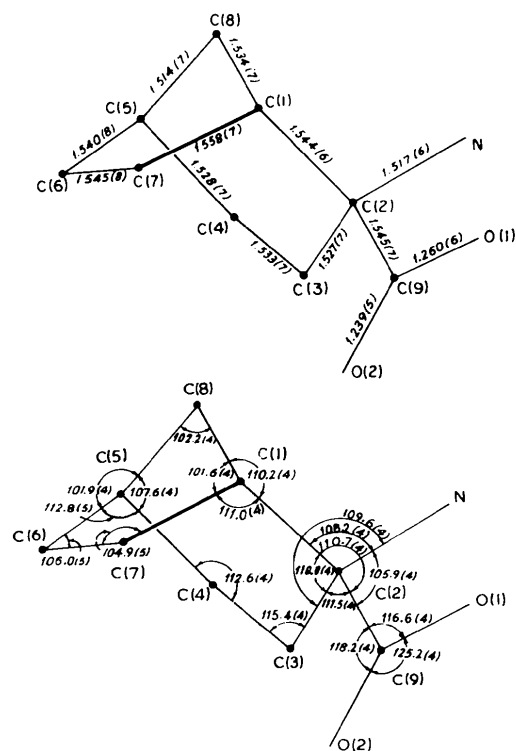


Fig. 2. Bond lengths (Å) and angles ($^\circ$) with their standard deviations.

edral value and it appears that the strain in these angles is somewhat relieved by the large C(2)–C(3)–C(4) angle of 115.4° of the three-atom bridge-head. The two C–C lengths [C(1)–C(8) 1.534 and C(5)–C(8) 1.514 Å] of the one-atom bridge-head are smaller than the three C–C bonds [C(1)–C(7) 1.558, C(6)–C(7) 1.545 and C(5)–C(6) 1.540 Å] of the two-atom bridge-head.

The bond lengths and angles show that the asymmetric substitution of the amino and carboxyl groups at the C(2) position disturbs the mirror symmetry of the bicyclo[3.2.1]octane system passing through C(3), C(8) and the middle of the C(6)–C(7) bond. The three C–C bonds to C(1) on the substituted side are significantly longer than the three to C(5) on the opposite side. A similar feature is seen in 2-BCH. Also, the C(8)–C(1)–C(2) angle of 110.2° is significantly larger than the 107.6° of C(8)–C(5)–C(4).

The bicyclo[3.2.1]octane system consists of five-, six- and seven-membered rings. Fig. 3 gives the torsion angles for these systems. The five-membered ring exists in an envelope conformation. C(1), C(7), C(6) and C(5) form a plane (plane 1), with C(8) 0.70 Å from the plane. The six-membered ring exists in a distorted chair conformation. For cyclohexane the expected torsion angle is $\pm 54.7^\circ$ (Bixon & Lifson, 1967). C(1), C(2), C(4) and C(5) form a plane (plane 2) with C(8) and C(3) on opposite sides by 0.49 and 0.86 Å respectively. The seven-membered ring exists in a distorted boat conformation. C(7), C(6) and C(3) deviate by 1.39, 1.39 and 0.49 Å respectively on the same side of the plane defined by C(1), C(2), C(4) and C(5) (plane 2). Table 4 gives the equations of the various least-

squares planes and atomic deviations. The torsion angles of the bicyclooctane system (Fig. 3) are also indicative of the breakdown of the mirror symmetry of the bicyclo[3.2.1]octane nucleus. The most significant torsion angles are those about C(1)–C(2) (-54.9°) and C(4)–C(5) ($+58.7^\circ$) of the six-membered ring, and about C(1)–C(2) ($+56.9^\circ$) and C(4)–C(5) (-52.9°) and about C(1)–C(7) (-90.4°) and C(5)–C(6) ($+86.1^\circ$) of the seven-membered ring. Each pair would have the same value for exact mirror symmetry.

The molecule exists as a zwitterion. The C(2)–N length of 1.517 Å is significantly larger than the 1.487 Å of Marsh & Donohue (1967). In 2-BCH this value is

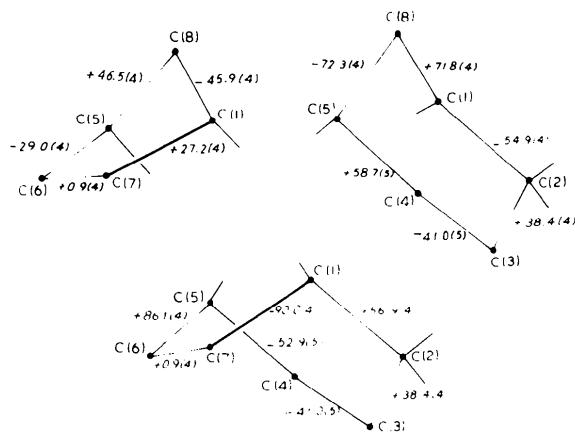


Fig. 3. Torsion angles ($^\circ$) of the bicyclo[3.2.1]octane system.

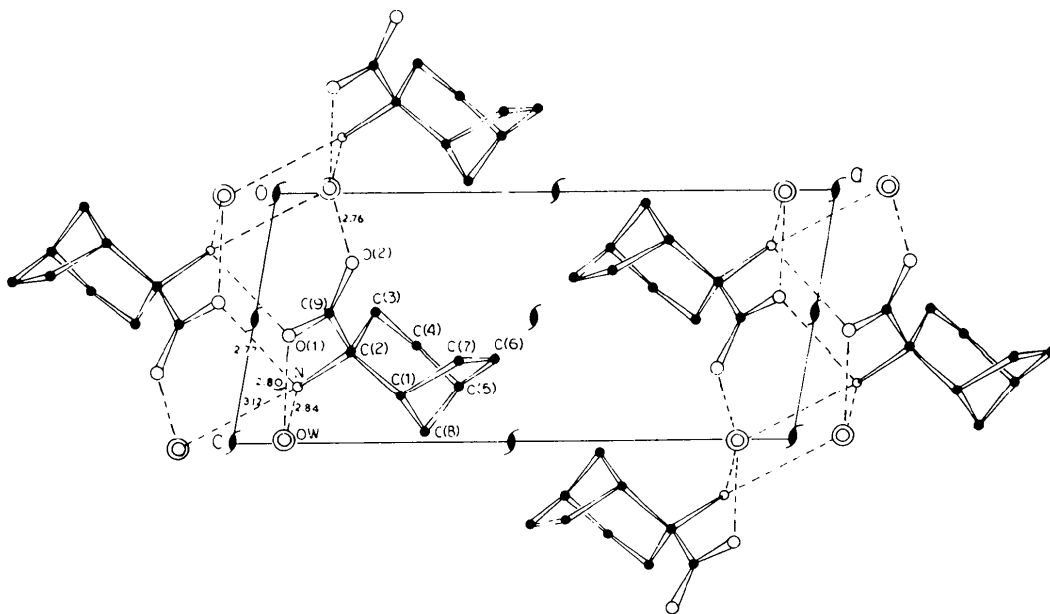


Fig. 4. Projection of the structure down *b*.

also large at 1.512 Å. C(9)—O(1), 1.260, and C(9)—O(2), 1.239 Å, differ, which presumably reflects the effects of hydrogen bonding. C(9)—O(1) is longer as O(1) is associated with two hydrogen bonds, one with the amino N and the other with the water O(W), while O(2) acts as acceptor of only one hydrogen bond from O(W). The carboxyl group [C(2), C(9), O(1) and O(2)] is planar; N deviates from this plane by 0.76 Å (Table 4, plane 3). The amino N is *exo* with respect to the bicyclo[3.2.1]octane system while the carboxyl group is *endo*.

Molecular packing and hydrogen bonding

A projection (for the correct absolute configuration) down **b** indicating the hydrogen bonds is shown in Fig. 4. The amino N which is in the NH₃⁺ state forms hydrogen bonds with O(W), O(W)^{iv} and O(1)ⁱⁱⁱ at distances of 2.84, 3.12 and 2.77 Å respectively (Table 5). N...O(W)^{iv} at 3.12 Å is a weak interaction as the H-acceptor distance is 2.49 Å. The projection down

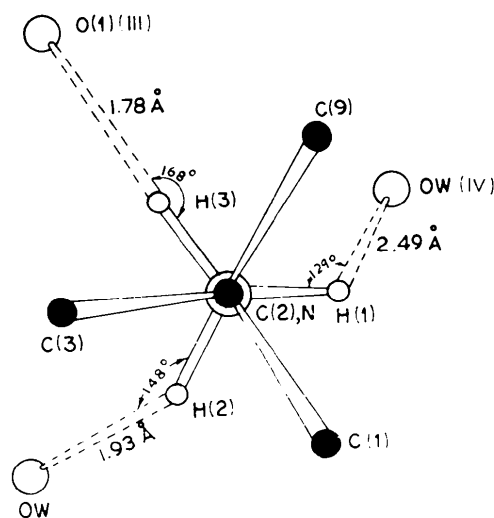


Fig. 5. Projection down C(2)—N.

Table 4. Least-squares plane calculations of 2-ABO and deviations (Å) of atoms from these planes

Plane 1: through C(1), C(5), C(6) and C(7)
 $0.437x + 0.203y + 0.876z = 5.172$

C(1)	-0.003	C(7)	0.005
C(5)	0.003	C(8)	-0.702
C(6)	-0.005		

Plane 2: through C(1), C(2), C(4) and C(5)
 $0.509x + 0.393y - 0.766z = -2.244$

C(1)	-0.012	C(3)	0.486
C(2)	0.011	C(8)	-0.863
C(4)	-0.011	C(6)	1.386
C(5)	0.012	C(7)	1.391

Plane 3: through C(2), C(9), O(1) and O(2)
 $0.688x + 0.586y + 0.428z = 2.238$

C(2)	-0.001	O(2)	-0.002
C(9)	0.005	N	0.755
O(1)	-0.002		

Table 5. Hydrogen-bond distances (Å) and angles (°)

C—D...A	D...A	H...A	D—H...A
N...O(W)	2.84	1.93	148
N...O(W) ^{iv}	3.12	2.49	129
N...O(1) ⁱⁱⁱ	2.77	1.78	168
O(W)...O(1) ^j	2.80	1.76	178
O(W)...O(2) ⁱⁱ	2.76	1.75	178

Symmetry code

(i)	$x, y - 1, z$	(iii)	$-x, \frac{1}{2} + y - 1, 1 - z$
(ii)	$x, y - 1, 1 + z$	(iv)	$-x, \frac{1}{2} + y, 2 - z$

C(2)—N (Fig. 5) shows that the hydrogen-bond directions are nearly staggered with respect to the bonds to C(2). The H atoms of the water molecule O(W) enter into two hydrogen bonds with O(1)^j and O(2)ⁱⁱ at 2.80 and 2.76 Å respectively. The water also accepts two hydrogen bonds from symmetry-related N atoms. The water molecule thus participates in four hydrogen bonds in a nearly tetrahedral arrangement.

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References

- APGAR, P. A. & LUDWIG, M. L. (1972). *J. Am. Chem. Soc.* **94**, 964–967.
 BIXON, M. & LIFSON, S. (1967). *Tetrahedron*, **23**, 769–784.
 CAHN, R. S., INGOLD, C. K. & PRELOG, V. (1956). *Experientia*, **12**, 81–94.
 CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
 DECLERCQ, J. P., GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1973). *Acta Cryst.* **A29**, 231–234.
 GANTZEL, P. K., SPARKS, R. A. & TRUEBLOOD, K. N. (1961). *UCLALS 1*, Univ. of California.
 HUGHES, E. W. (1941). *J. Am. Chem. Soc.* **63**, 1737–1752.
International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.
 MARSH, R. E. & DONOHUE, J. (1967). *Adv. Protein Chem.* **22**, 235–256.
 ZAND, R., SELINGER, O. Z., WATER, R. & HARRIS, R. (1974). *J. Neurochem.* **23**, 1201–1206.
 ZAND, R. & WATER, R. (1977). Unpublished results.