

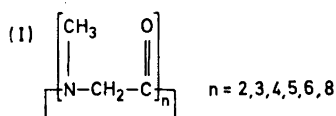
## Crystal Structure of Cyclotetrasarcosyl

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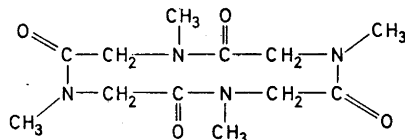
The crystals belong to the monoclinic system with space group  $P2_1/c$  and cell dimensions  $a=7.19$ ,  $\text{\AA}$ ,  $b=8.38$ ,  $\text{\AA}$ ,  $c=11.17$ ,  $\text{\AA}$ ,  $\beta=89.9_1^\circ$ . There are two molecules in the unit cell. The phase problem was solved by a computer procedure based on direct methods. The  $R$ -value arrived at for 1204 observed reflections was 7.8%. Corresponding bond distances of the *cis* and *trans* parts of the molecule are equal within probable limits of error. None of the amide groups are strictly planar. In the *cis* part the *internal* C—N—C angle is opened ( $123.9^\circ$ ), while one of the *external* C—N—C angles is opened ( $124.3^\circ$ ) in the *trans* part. The shortest transannular distance is  $N\cdots C(\text{carbonyl})$  of  $3.08$ ,  $\text{\AA}$  between the two *trans* groups.

Cyclic oligopeptides of sarcosine of the general formula



have been studied by Dale and Titlestad.<sup>1</sup> To account for the relatively high observed resistance to ring inversion, transannular interactions between N and C (carbonyl) are suggested. Such interactions have been reported to exist in certain cyclic aminoketones.<sup>2</sup> In the 10-ring lactone of 6-keto-9-hydroxy-nonanoic acid<sup>3</sup> there is strong evidence for transannular donor-acceptor attraction between the "ether" oxygen of the ester group and the carbonyl carbon atom. Several examples of *intermolecular*  $O\cdots C$  interactions of this kind have also been observed.<sup>4-6</sup>

In order to establish whether transannular  $N\cdots C$  (carbonyl) attractions actually are stabilising the oligomers (I), and to obtain detailed information about the conformations of the *cis*- and *trans*-amide groups, single crystals of some of these compounds are being examined by X-ray methods. The case  $n=2$  has recently been solved,<sup>7</sup> and now the results of the crystal structure determination of cyclotetrasarcosyl ( $n=4$ ) are presented.



The crystals belong to the monoclinic system and the systematic absences lead to the space group  $P2_1/c$ . The cell parameters,<sup>8\*</sup> measured by means of a four circle diffractometer, and their estimated standard deviations are:

$$a = 7.198(2) \text{ \AA}, \quad b = 8.386(2) \text{ \AA}, \quad c = 11.174(2) \text{ \AA}, \quad \beta = 89.91(1)^\circ$$

The unit cell contains two molecules ( $\rho_{\text{calc}} = 1.40 \text{ g} \cdot \text{cm}^{-3}$ ,  $\rho_{\text{obs}} = 1.40 \text{ g} \cdot \text{cm}^{-3}$ ).

Intensity data were obtained by photometric measurements of integrated equiinclination Weissenberg diagrams corresponding to  $0kl$ ,  $h0l$ ,  $\dots$ ,  $h7l$ . 1204 independent reflections were strong enough to be measured. No corrections have been made for absorption or secondary extinction effects.

The phase problem was solved three-dimensionally by a computer procedure based on direct methods. 269 signs were determined (all of which turned out to be correct), and the corresponding Fourier map contained 10 peaks with heights ranging from  $5 \text{ e} \cdot \text{\AA}^{-3}$  to  $9 \text{ e} \cdot \text{\AA}^{-3}$  which clearly showed the molecule.

The refinement was carried out by full-matrix least squares technique. The weighting scheme: for  $F_o \leq FB$ ,  $W = A1 \cdot (F_o)^{B1}$ ; for  $F_o > FB$ ,  $W = A2 \cdot (F_o)^{B2}$  was used with  $A1 = 10.0$ ,  $A2 = 13.0$ ,  $B1 = 0.0$ ,  $B2 = -0.5$  and  $FB = 1.7$ . The atomic form factors were those of Hanson *et al.*<sup>9</sup> except for hydrogen.<sup>10</sup>

Methylene hydrogen positions were calculated assuming tetrahedral C—H bonds of length  $1.03 \text{ \AA}$ . Four methyl hydrogens could be localized from a difference Fourier map while the positions of the remaining two were calculated under the same assumptions as above. All hydrogen atoms were given the same isotropic temperature factor  $B = 5.0 \text{ \AA}^2$ , and only the positional parameters were refined.

The  $R$ -value arrived at for 1204 observed reflections was  $7.8 \%$ . A final difference Fourier map, calculated with the phases determined by the parameters corresponding to  $R = 7.8 \%$ , contained no larger density fluctuations than  $\pm 0.30 \text{ e} \cdot \text{\AA}^{-3}$ .

The fractional atomic coordinates and the thermal vibration parameters arrived at are given in Tables 1 and 2. The expression for anisotropic vibrations is:

$$\exp[-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)]$$

A comparison between calculated and observed structure factors is presented in Table 3.

The principal axes of the thermal vibration ellipsoids for oxygen, nitrogen, and carbon atoms were calculated from the temperature parameters of Table 1. Root mean square amplitudes and the corresponding  $B$ -values for the atomic anisotropic thermal vibrations along the principal axes together with the components of these axes along the crystal axes are given in Table 4.

\* All programs used are included in this reference.

Table 1. Fractional atomic coordinates and anisotropic thermal vibration parameters with estimated standard deviations (multiplied by  $10^5$ ).<sup>a</sup>

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> <sub>11</sub>	<i>B</i> <sub>22</sub>	<i>B</i> <sub>33</sub>	<i>B</i> <sub>12</sub>	<i>B</i> <sub>13</sub>	<i>B</i> <sub>23</sub>
O <sub>1</sub>	03636 27	23656 28	50918 19	1643 44	1125 44	831 20	50 54	-97 44	-345 37
O <sub>2</sub>	44031 34	-12978 34	26502 21	2115 53	1898 51	808 20	1417 76	712 50	-140 46
N <sub>1</sub>	06224 30	07575 30	34791 19	1367 45	1095 47	627 18	520 59	147 42	42 36
N <sub>2</sub>	33155 32	-16611 32	45217 21	1374 44	1261 50	758 21	933 63	160 44	-193 42
C <sub>1</sub>	-03561 35	14975 33	43623 22	1373 49	789 48	598 20	444 64	-13 46	129 42
C <sub>2</sub>	35285 36	-07893 40	35184 26	1120 46	1410 59	775 24	423 72	135 51	-230 49
C <sub>3</sub>	26415 43	08608 43	34520 33	1409 55	1365 63	947 28	-23 81	595 60	317 59
C <sub>4</sub>	24174 36	-10767 41	55981 25	1256 49	1255 60	650 22	711 67	-142 49	-145 45
C <sub>5</sub>	-02187 47	-01997 52	25257 28	1899 64	1918 80	662 25	928 103	-365 58	-387 59
C <sub>6</sub>	39819 54	-33020 48	45544 34	2171 73	1404 72	926 30	1538 102	-80 73	-319 61

<sup>a</sup> For numbering of atoms, see Fig. 1.

Table 2. Fractional atomic coordinates for the hydrogen atoms. (H<sub>m,n</sub> is bonded to C<sub>m</sub>).

Atom	<i>x</i>	<i>y</i>	<i>z</i>
H <sub>3,1</sub>	.287	.139	.271
H <sub>3,2</sub>	.319	.152	.400
H <sub>4,1</sub>	.295	-.156	.631
H <sub>4,2</sub>	.261	.016	.566
H <sub>5,1</sub>	-.006	.031	.175
H <sub>5,2</sub>	.035	-.131	.258
H <sub>5,3</sub>	-.163	-.051	.261
H <sub>6,1</sub>	.433	-.368	.526
H <sub>6,2</sub>	.287	-.410	.429
H <sub>6,3</sub>	.464	-.362	.412

The results of a rigid-body analysis of translational and librational motion of the molecule about the centre of symmetry are given in Table 5. The **T** and **L** tensors are calculated in an orthogonal coordinate system, *L, M, N*, defined by the principal inertial axes of the molecule. The largest r.m.s.







Table 4. The principal axes of the thermal vibration ellipsoids given by the components of a unit vector in fractional coordinates  $e_x$ ,  $e_y$ ,  $e_z$ ; the corresponding r.m.s. amplitudes, and the  $B$ -values.

Atoms	$e_x$	$e_y$	$e_z$	$(\bar{u}^2)^{\frac{1}{2}}$ (Å)	$B$ (Å <sup>2</sup> )
O <sub>1</sub>	.020	.052	-.079	.239	4.50
	.137	-.010	.011	.207	3.38
	.003	.107	.040	.190	2.84
O <sub>2</sub>	.089	.089	.018	.292	6.74
	.044	-.059	.072	.243	4.66
	-.097	.054	.050	.173	2.37
N <sub>1</sub>	.086	.083	.033	.216	3.68
	.015	.047	-.082	.197	3.07
	-.108	.072	.015	.170	2.29
N <sub>2</sub>	.075	.096	-.022	.236	4.41
	.045	.008	.085	.221	3.85
	-.108	.070	.020	.156	1.92
C <sub>1</sub>	.099	.060	.044	.202	3.21
	.072	.011	-.076	.194	2.97
	.066	-.102	.017	.154	1.87
C <sub>2</sub>	.018	.094	-.054	.236	4.38
	.046	.064	.069	.215	3.66
	-.130	.036	.017	.163	2.11
C <sub>3</sub>	.048	.041	.078	.260	5.34
	.044	-.110	.021	.216	3.70
	.123	.024	-.038	.176	2.45
C <sub>4</sub>	.068	.095	-.032	.230	4.17
	.019	.039	.084	.199	3.12
	.120	-.060	.004	.163	2.09
C <sub>5</sub>	.065	.099	-.026	.282	6.28
	-.104	.066	.033	.207	3.39
	.066	.005	.079	.194	1.96
C <sub>6</sub>	.098	.077	-.026	.281	6.25
	.045	.008	.084	.240	4.54
	-.087	.091	.015	.170	2.29

amplitude of angular oscillation, 4.49°, is about a direction close to that of the  $L$ -axis, corresponding to the smallest moment of inertia. The r.m.s. discrepancy between atomic vibration tensor components,  $U_{ij}$ , calculated from the thermal parameters of Table 1, and those calculated with the rigid-body parameters, serves as a measure of the applicability of the analysis and thus of the rigidity of the molecule. The value of Table 5, 0.0030 Å<sup>2</sup>, supports the assumption of regarding the molecule as an oscillating rigid body, and the fractional coordinates were accordingly corrected for librational effects.<sup>11</sup> Table 6 shows that the largest corrections are about three times the corresponding standard deviations.

Table 5. Principal moments of inertia of the molecule (a.m.u. Å<sup>2</sup>), unit vectors along the principal axes, *L, M, N*, defining the molecular coordinate system, and the rigid-body tensors referred to this coordinate system.

Axis	Moment	$e_x$	$e_y$	$e_z$
L	441.9	.109	-.048	-.042
M	998.3	.021	-.073	.069
N	1197.5	.084	.081	.038

$$T = \begin{pmatrix} 230 & -49 & 15 \\ & 374 & -17 \\ & & 283 \end{pmatrix} \times 10^{-4} \text{ Å}^2$$
  

$$L = \begin{pmatrix} 60 & 6 & -2 \\ & 25 & 4 \\ & & 15 \end{pmatrix} \times 10^{-4} \text{ rad.}^2$$
  

	r.m.s. amplitudes	Direction cosines		
		<i>L</i>	<i>M</i>	<i>N</i>
T	.200 Å	.4466	.4315	.7838
	.168 »	-.8767	.3858	.2872
	.165 »	.1784	.8154	-.5506
L	4.49°	.9856	.1441	.0881
	2.91°	.1650	-.9321	-.3224
	2.09°	-.0357	-.3323	.9425

$$\left( \frac{1}{\Delta U_{ij}^2} \right)^{\frac{1}{2}} = 0.0030 \text{ Å}^2$$

Table 6. Libration corrections in fractional atomic coordinates compared with estimated standard deviations in coordinates ( $\sigma$ 's and  $\Delta$ 's are multiplied by 10<sup>5</sup>).

Atom	$\Delta x$	$\sigma(x)$	$\Delta y$	$\sigma(y)$	$\Delta z$	$\sigma(z)$
O <sub>1</sub>	39	27	89	28	0	19
O <sub>2</sub>	92	34	0	34	-65	21
N <sub>1</sub>	15	30	39	30	-53	19
N <sub>2</sub>	72	32	30	32	-2	21
C <sub>1</sub>	2	35	54	33	-27	22
C <sub>2</sub>	80	36	8	40	-39	26
C <sub>3</sub>	74	43	60	43	-47	33
C <sub>4</sub>	62	36	-20	41	32	25
C <sub>5</sub>	-29	47	0	52	-88	28
C <sub>6</sub>	72	54	-84	48	5	34

Interatomic distances and bond angles (corrected for libration) with estimated standard deviations may be found in Fig. 1, where the molecule is viewed along [010]. The standard deviations have been calculated from the correlation matrix corresponding to the last full-matrix least squares refinement cycle.



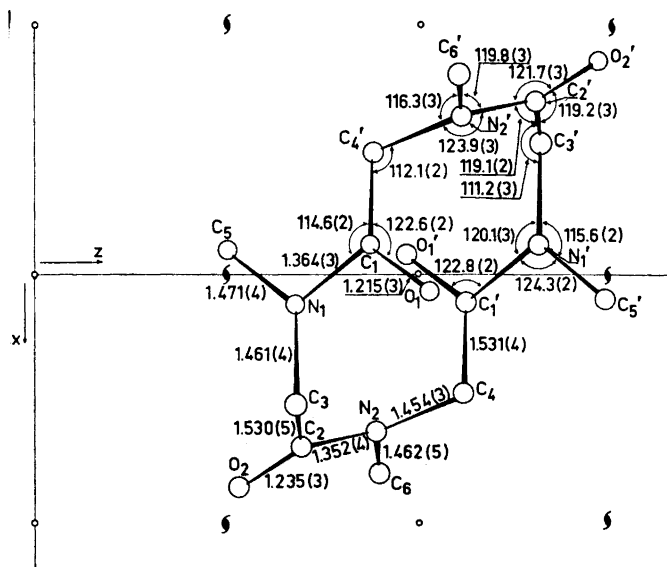
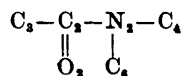
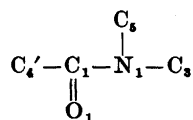


Fig. 1. Schematic drawing of the molecule (viewed along [010]) showing bond distances and angles.

Fig. 1 shows that corresponding bond distances of the *cis* part:



and the *trans* part:



of the molecule are equal within probable limits of error (except for  $\text{C}_2-\text{O}_2$  (1.235 Å) which is *possibly significantly* longer than  $\text{C}_1-\text{O}_1$  (1.215 Å)). The mean values agree fairly well with the results obtained for *N,N'*-dimethyl-diketopiperazine:<sup>7</sup>

Distance (Å)	<i>N,N'</i> -dimethyl-diketopiperazine	Present compound
C (carbonyl) — C (methylene)	1.506	1.531
C (carbonyl) — N	1.348	1.358
C (carbonyl) — O	1.234	1.225
C (methylene) — N	1.455	1.458
C (methyl) — N	1.475	1.467

Some of the corresponding bond angles, however, differ significantly. In the *trans* amide group the *external* angle  $C_1-N_1-C_5$  is opened ( $124.3^\circ$ ), while  $\angle C_3-N_1-C_5=115.6^\circ$  and the *internal* angle  $\angle C_1-N_1-C_3=120.1^\circ$ . In the *cis* amide group the *internal* angle  $C_2-N_2-C_4$  is opened ( $123.9^\circ$ ), while  $\angle C_4-N_2-C_6=116.3^\circ$  and  $\angle C_2-N_2-C_6=119.8^\circ$ . The corresponding three angles in the (*cis*) amide group of *N,N'*-dimethyl-diketopiperazine are  $124.6^\circ$ ,  $115.5^\circ$ , and  $119.7^\circ$ , respectively.

The dihedral angles of Table 7 show that both [C-N-C] groups are planar,

$$\begin{array}{c} | \\ C \\ | \\ \text{the distance from the least squares plane being less than } 0.006 \text{ \AA. The} \\ \text{[C-C-N] group of the } cis \text{ part is also essentially planar (greatest deviation} \\ \parallel \\ O \end{array}$$

0.004 Å). However, the corresponding group in the *trans* part seems to be slightly pyramidal, with  $C_1$  displaced by 0.017 Å from the least squares plane and the other atoms 0.005 Å in the opposite direction.  $C_1$  is somewhat *inside* the ring. It should be pointed out that the angle  $C_4'-C_1-N_1$  of  $114.6^\circ$  is significantly smaller than the other two angles at  $C_1$  ( $122.6^\circ$  and  $122.8^\circ$ ). No such effect is observed at  $C_2$ . Although the direction of displacement of  $C_1$  indeed is towards  $N_1'$ , considerations of probable limits of error together with the fact that the distance  $C_1 \cdots N_1'$  is as long as 3.083 Å, do not allow any conclusions concerning stabilising transannular  $N \cdots C$  attractions to be drawn with confidence. All other transannular distances as well as *intermolecular* contacts correspond at least to van der Waals distances.

Table 7. Dihedral angles with estimated standard deviations.

Angle	(°)
$C_4'-C_1-N_1-C_5$	8.1 (4)
$C_3-C_2-N_2-C_6$	173.5 (3)
$C_4'-C_1-N_1-C_3$	-170.6 (3)
$C_3-C_2-N_2-C_4$	-5.4 (4)
$C_1-N_1-C_3-C_2$	120.8 (3)
$N_1-C_3-C_2-N_2$	-65.5 (4)
$C_2-N_2-C_4-C_1'$	93.6 (4)
$N_2-C_4-C_1'-N_1'$	-169.5 (2)
$O_1-C_1-N_1-C_5$	-175.0 (3)
$O_2-C_2-N_2-C_6$	-5.7 (5)
$C_5-N_1-C_3-C_2$	-58.1 (4)
$C_6-N_2-C_4-N_1'$	-151.0 (2)
$N_1-C_3-C_2-O_2$	113.7 (3)
$N_2-C_4-C_1'-O_1'$	68.7 (2)
Angle between the planes	(°)
$C_4'-C_1-O_1$ and $O_1-C_1-N_1$	3.4 (5)
$C_3-C_2-O_2$ and $O_2-C_2-N_2$	0.8 (5)
$C_1-N_1-C_5$ and $C_5-N_1-C_3$	1.2 (4)
$C_2-N_2-C_6$ and $C_6-N_2-C_4$	1.0 (4)

As may be seen from Table 7, the amide groups are not strictly planar. The deviations of C<sub>3</sub>,C<sub>5</sub> from the plane O<sub>1</sub>,C<sub>1</sub>,N<sub>1</sub> and C<sub>4</sub>,C<sub>6</sub> from the plane O<sub>2</sub>,C<sub>2</sub>,N<sub>2</sub>, respectively, are all about 0.1 Å.

The dihedral angle (in the ring) of the C—C single bond is roughly normal for full carbonyl double bond both in the *cis* (−65.5°) and *trans* (−169.5°) group. The dihedral (ring) angle of the C—N single bond of the *trans* group (120.8°) corresponds closely to a full C(carbonyl)—N double bond. In the *cis* part the corresponding angle has the intermediate value 93.6°.

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