

The Structure of *N*-Methyl-5,5-dimethyloxazolidine-2,4-dione*

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The X-ray crystal structure of *N*-methyl-5,5-dimethyloxazolidine-2,4-dione ($C_6O_3NH_9$) has been determined by the application of the direct method procedure. The crystals are monoclinic, space group $P2_1/c$ (C_{2h}^5), with four molecules in a unit cell of dimensions $a = 6.449$, $b = 6.032$, $c = 19.639$ Å and $\beta = 97.95^\circ$. The basic five-membered oxazolidine ring is nearly planar. Two of the methyl groups are ordered, while the *N*-methyl group shows two preferred orientations. Full-matrix least-squares refinement gave a final weighted R index of 5.1% based on 1011 counter collected reflections.

Introduction

Oxazolidinones and their metal chelates have been the subject of several recent investigations (Lange, Candon & Chessin, 1962; Glasky & Simon, 1966; Plotnikoff, 1966*a, b*; Morris, Aghayanian & Bloom, 1967; Stein & Yellin, 1967). These compounds are of interest because of their reported effects on behavior patterns and their somewhat disputed interaction with brain ribonucleic acid polymerase. We have undertaken a structural investigation of the oxazolidinones and their metal chelates, and we report here the results of a single-crystal X-ray investigation of the structure of *N*-methyl-5,5-dimethyloxazolidine-2,4-dione.

Experimental

A sample of *N*-methyl-5,5-dimethyloxazolidine-2,4-dione (TRIDIONE®) was obtained through the courtesy of Dr W. J. Close, Abbott Laboratories, Scientific Divisions, North Chicago, Illinois. Suitable crystals for X-ray investigation were grown from reagent grade tetrahydrofuran by slow evaporation of the solvent.

The crystals are monoclinic, and systematic absences as determined from precession ($Mo K\alpha$) and Weissenberg ($Cu K\alpha$) photographs were: $h0l$, $l \neq 2n$; $0k0$, $k \neq 2n$. These absences are consistent with the centrosymmetric space group $P2_1/c$ (C_{2h}^5). Lattice constants and standard deviations obtained by a least-squares fit to the angular settings of 12 reflections carefully centered on a Picker four-circle diffractometer are: $a = 6.449 \pm 0.002$, $b = 6.032 \pm 0.001$, $c = 19.639 \pm 0.005$ Å, $\beta = 97.95 \pm 0.04^\circ$, and $V = 756.51$ Å³ (28°C, $\lambda(Cu K\alpha_1) 1.54051$ Å). The density measured by pycnometric techniques using *n*-hexane is 1.31 ± 0.02 g.cm⁻³, while that calculated for four molecules per unit cell is 1.26 g.cm⁻³. The high solubility of the compound in common organic solvents necessitated a rapid, somewhat inaccurate density measurement.

Intensity data were collected on an automated Picker four-circle diffractometer (Ni-filtered $Cu K\alpha$ radiation). The data were collected by the $\theta - 2\theta$ scan technique to a maximum 2θ of 115° . The take-off angle was set at 2° , or approximately 75% of the maximum intensity obtained by measuring the intensity of a reflection as a function of take-off angle. A scan rate of 1° min^{-1} was used throughout data collection, and stationary background counts for 10 sec were taken at the beginning and the end of the scan. Two symmetry related forms (hkl , $h\bar{k}l$ and hkl , $h\bar{k}\bar{l}$) were collected and averaged. Two standard reflections were monitored every 40 reflections during data collection. No single observation of their integrated intensities differed by more than 3% from its average value. Unobserved reflections [$(I_0 < 3(\sigma^2(I) + \sigma^2(BKG)))^{1/2}$, where I_0 is the background corrected intensity, $\sigma^2(I)$ is the total integrated peak count in a scan of time TC , and $\sigma^2(BKG) = (TC/TB)^2(B_1 + B_2)$, with B_1 and B_2 the background counts in a time $TB/2$, were given a raw intensity of $(\sigma^2(I) + \sigma^2(BKG))^{1/2}$. One reflection 054 was rejected from the data set as being statistically unreliable: $I_0 < [I_{BKG} - 3\sigma(BKG)]$. The two symmetry related sets of measurements reduced to 1011 independent reflections of which 171 were assigned as unobserved by the criterion given above.

The crystal used for data collection was a block $0.40 \times 0.34 \times 0.21$ mm. The calculated linear absorption coefficient for $Cu K\alpha$ radiation is 9.04 cm^{-1} . The maximum error in the intensities due to neglect of the absorption correction was estimated to be 8%. Corrections were made for Lorenz and polarization effects. The scattering factors C, N and O were taken from the compilation of Hanson, Herman, Lea & Skillman (1964). The spherical scattering factors for H were those of Stewart, Davidson & Simpson (1965).

Structure determination and refinement

The normalized structure factor magnitudes $|E|$ were calculated from the observed structure factors $|F|$ by application of the K curve method (Karle & Hauptman, 1953; Patterman, 1969). The phase determining algo-

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rithms \sum_1 and \sum_2 for $P2_1/c$ (Hauptman & Karle, 1954) were used in the phase determining process. Application of \sum_1 relationships led to starting signs for two reflections (4 0 18, 4 0 6). Three reflections were assigned signs to specify the origin. This basic starting signs was then expanded by the \sum_2 algorithm. In order to obtain signs for a sufficient number of high $|E|$ values, it was found necessary to assign symbolic phases to two further reflections. The reflections determined by \sum_1 , those used to assign the origin, and the two given symbolic phases (*A* and *B*) are listed in Table 1. There were strong indications from the \sum_2 interactions that *A* was positive and *B* negative. With this set of 7 signed $|E|$ values, a total of 96 reflections were assigned signs by application of \sum_2 . An *E* map (Karle, Hauptman, Karle & Wing, 1958; Gvildys, 1968) with these 96 reflections as coefficients revealed the positions of all 10 heavy atoms (C, N, O). Only one spurious peak was found, and it was easily eliminated by consideration of normal bonded distances.

Table 1. Summary of the reflections used in the phasing process

<i>h</i>	<i>k</i>	<i>l</i>	$ E $	<i>S</i>	<i>P</i> ₊	Mode of selection
4	0	18	2.148	—	0.12	\sum_1
4	0	6	1.879	+	0.76	\sum_1
3	0	6	2.704	+		origin
3	4	7	2.787	+		origin
1	3	8	2.718	+		origin
2	2	18	2.660	<i>A</i>		symbolic (\sum_2)
3	3	1	2.638	<i>B</i>		symbolic (\sum_2)

The atomic coordinates and thermal parameters of these 10 major atoms were refined by full-matrix least-squares using the program *ORFLS* (Busing, Martin & Levy, 1962). The function minimized was $\sum w(F_o - F_c)^2$. At the termination of anisotropic refinement the error factors were:

$$R_1 = \sum |F_o| - |F_c| / \sum |F_o| = 0.077,$$

and

$$R_2 = [\sum w(F_o - F_c)^2 / \sum F_o^2]^{1/2} = 0.111$$

for the observed data. The weights [$w = 1/\sigma^2(F)$] were chosen from a modified Hughes scheme (Hughes, 1941; Abrahams & Reddy, 1965; Abrahams, 1969): $F \leq 4F_{\min}$, $\sigma(F) = 1$; $F > 4F_{\min}$, $\sigma(F) = F/5F_{\min}$, where F_{\min} was taken as the magnitude of the minimum observed reflection.

A three-dimensional difference Fourier synthesis (Gvildys, 1968) was calculated in an attempt to locate the 9 hydrogen atoms. The methyl protons associated with carbon atoms C(7) and C(8) (see Fig. 1) were easily located. Their maximum peak values ranged from 0.38 to 0.59 e.Å⁻³. The hydrogen atoms associated with the *N*-methyl carbon atom [C(6), see Fig. 1] gave evidence of being disordered about the potential mirror of the oxazolidine ring. Position parameters for six essentially $\frac{1}{2}$ hydrogen atoms (ρ_{\max} ranging from 0.21 to 0.34 e.Å⁻³) were calculated. In the remaining cycles of refinement, the hydrogen atoms on C(7) and C(8) were allowed to

Table 2. Positional and thermal parameters for the nonhydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>	$\langle U_{11} \rangle^\dagger$	<i>B</i> ₂₂	<i>B</i> ₃₃	<i>B</i> ₁₂	<i>B</i> ₁₃	<i>B</i> ₂₃
N	0.0892 (2)*	0.0884 (3)	0.3425 (1)	0.0201 (4)	0.0272 (6)	0.0025 (1)	0.0011 (4)	0.0014 (1)	0.0008 (1)
O(1)	0.2453 (2)	0.1797 (3)	0.3485 (1)	0.0212 (4)	0.0335 (5)	0.0029 (1)	0.0007 (3)	0.0018 (1)	0.0021 (1)
C(2)	0.0913 (3)	0.0623 (3)	0.3127 (1)	0.0225 (5)	0.0233 (6)	0.0024 (1)	0.0020 (5)	0.0017 (1)	0.0001 (2)
O(2)	0.1120 (2)	0.0467 (3)	0.2634 (1)	0.0322 (5)	0.0327 (5)	0.0029 (1)	0.0016 (4)	0.0028 (1)	0.0026 (1)
C(4)	0.0595 (3)	0.2340 (4)	0.3957 (1)	0.0237 (6)	0.0296 (7)	0.0023 (1)	0.0030 (5)	0.0018 (1)	0.0001 (2)
O(4)	0.1912 (2)	0.2979 (3)	0.4294 (1)	0.0299 (5)	0.0555 (7)	0.0039 (1)	0.0014 (5)	0.0043 (1)	0.0050 (2)
C(5)	0.1691 (3)	0.2979 (3)	0.4051 (1)	0.0234 (5)	0.0278 (7)	0.0023 (1)	0.0012 (5)	0.0013 (1)	0.0010 (2)
C(6)	0.2894 (4)	0.0096 (6)	0.3137 (2)	0.0235 (7)	0.0509 (11)	0.0043 (1)	0.0079 (7)	0.0019 (1)	0.0040 (3)
C(7)	0.2012 (5)	0.5427 (4)	0.3956 (1)	0.0441 (9)	0.0292 (8)	0.0031 (1)	0.0054 (7)	0.0010 (2)	0.0005 (2)
C(8)	0.2819 (5)	0.2125 (5)	0.4721 (1)	0.0335 (8)	0.0413 (11)	0.0028 (1)	0.0039 (7)	0.0005 (2)	0.0001 (2)

* Numbers in parentheses here and in succeeding Tables are estimated standard deviations in the least significant digits.
 † The form of the anisotropic ellipsoid is $\exp [-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + 2B_{12}hk + 2B_{13}hl + 2B_{23}kl)]$.

B value for the disordered hydrogen atoms was taken as the average of those of the ordered hydrogen atoms. The final error factors based on 133 parameters including one scale factor and 1011 reflections were $R_1=0.043$ (observed data) and $R_2=0.051$ (observed and unobserved data). The estimated standard deviation of an observation of unit weight was 0.93. Table 2 lists the final positional and thermal parameters for the nonhydrogen atoms, and Table 3 those for the hydrogen atoms. The observed and calculated structure factor amplitudes are collected in Table 4. A final difference Fourier synthesis showed no spurious peaks above $0.15 \text{ e.}\text{\AA}^{-3}$.

Discussion

Fig. 1 is a representation of the molecular geometry and the anisotropic thermal motion in *N*-methyl-5,5-dimethyloxazolidine-2,4-dione. The associated root-mean-square amplitudes of vibration for the major atoms are collected in Table 5. The basic oxazolidine ring is nearly planar. The nitrogen atom shows the maximum deviation (0.08 \AA) from the least-squares plane (Table 6). The internal ring distances and angles (Table 7) differ in two main features from those reported by Turley (1969) for 2-oxazolidinone:

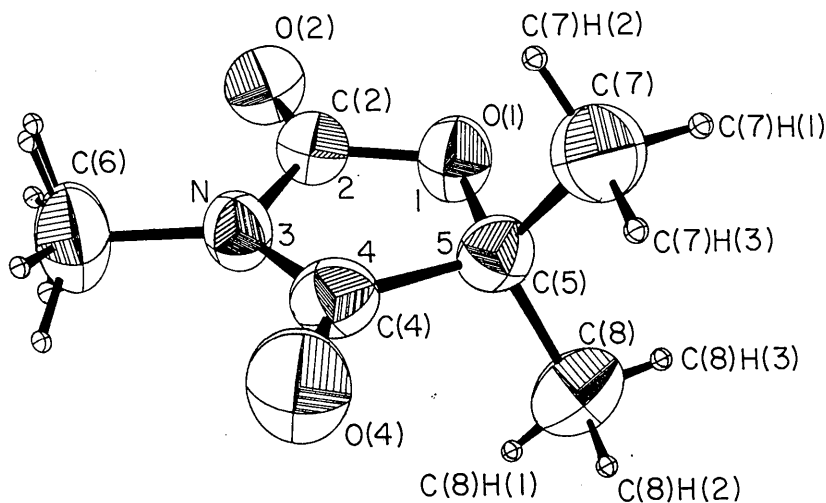


Fig. 1. A perspective view of the molecular geometry showing ellipsoids of thermal motion.

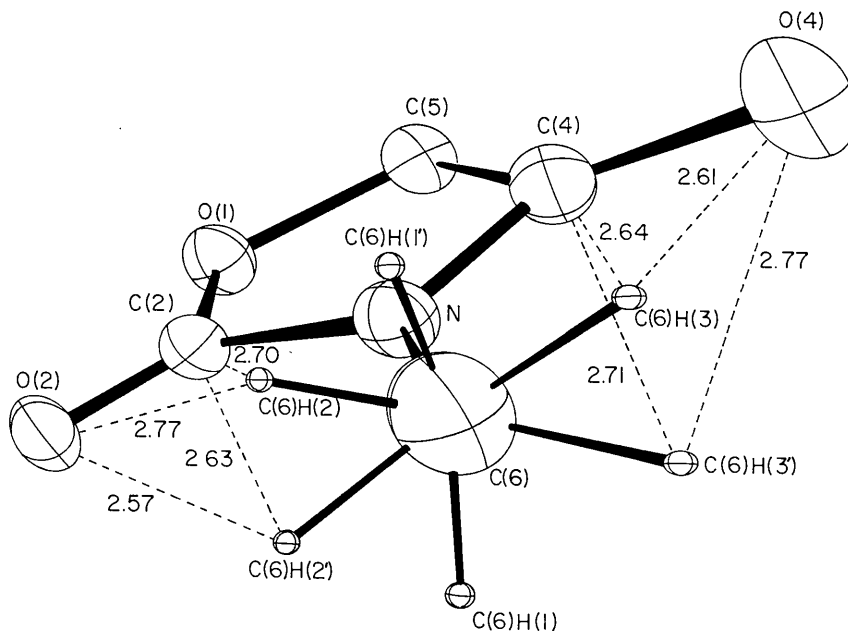


Fig. 2. A view of the disordered methyl group and its interactions.

- (1) the angle about C(4) has opened from 99.8 to 106.9 (2)° and at C(5) has closed from 106.0 to 102.0 (2)°;
- (2) the N-C(2) and N-C(4) distances are nearly equivalent [1.357 (3) and 1.383 (3) Å] while those in 2-oxazolidinone are considerably different (1.304 and 1.466 Å).

Both of these effects can be ascribed to the substitution of the carbonyl function for the methylene group at ring position (4).

Table 5. *Root-mean-square amplitudes of vibration along the principal axes, R_i*

(See Fig. 1.)

	R_1	R_2	R_3
N	0.200 (2) Å	0.211 (2) Å	0.233 (2) Å
O(1)	0.201 (2)	0.219 (2)	0.268 (2)
O(2)	0.194 (2)	0.260 (2)	0.274 (2)
O(4)	0.196 (2)	0.273 (2)	0.349 (2)
C(2)	0.198 (3)	0.209 (3)	0.226 (3)
C(4)	0.198 (3)	0.222 (3)	0.242 (3)
C(5)	0.197 (3)	0.221 (2)	0.234 (3)
C(6)	0.209 (3)	0.258 (3)	0.337 (4)
C(7)	0.224 (3)	0.247 (3)	0.308 (3)
C(8)	0.220 (3)	0.265 (3)	0.290 (3)

Table 6. *Least-squares plane and deviations*

	Deviation		Deviation
N	-0.083 (2) Å	*O(4)	0.012 (2) Å
*O(1)†	0.011 (2)	*C(5)	-0.006 (2)
*C(2)	-0.016 (2)	C(6)	-0.060 (4)
*O(2)	0.007 (2)	C(7)	1.241 (2)
*C(4)	-0.018 (2)	C(8)	-1.264 (3)

† Equation of the plane: $-0.1262X + 0.7893Y - 0.6009Z = 3.3086$, where X , Y and Z are coordinates (Å) referred to the orthogonal axes a , b and c^* .

‡ Atoms used to define the least-squares plane are preceded by an asterisk. The contribution of each atom in the least-squares analysis was weighted by $3/[\sigma^2(x) + \sigma^2(y) + \sigma^2(z)]$.

The hydrogen atoms have been refined successfully to chemically and geometrically acceptable bonded distances and angles (Table 8). The potential mirror about which the N -methyl group [C(6)] has disordered is clearly shown in Fig. 2 where a summary of the short-

est interaction distances is also given. The closing of the ring angle at C(5) has led to the opening of the opposite external angle [C(7)-C(5)-C(8), 112.7 (2)°]. The opening of this angle has caused the methyl group, C(7), to stagger about the ring oxygen atom and the methyl group, C(8), to stagger about O(4). These methyl groups, C(7) and C(8), have then assumed an eclipsed conformation [C(7)H(1)-C(8)H(3), 2.51 (5), C(7)H(3)-C(8)H(2), 2.50 (4) Å] with slightly longer than normal van der Waals contacts. A view down [010] of the molecular packing is given in Fig. 3.

Further structural studies on the oxazolidinones and their metal chelates are in progress. A discussion of the chemical significance of the structural results will be given in a later article.

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Table 7. *Bond lengths and angles for the nonhydrogen atoms*

Bond lengths		Bond angles	
N—C(2)	1.383 (3) Å	C(2)—N—C(4)	111.2 (2)°
N—C(4)	1.357 (3)	C(2)—N—C(6)	122.7 (2)
N—C(6)	1.461 (3)	C(4)—N—C(6)	125.7 (2)
O(1)—C(2)	1.337 (3)	C(2)—O(1)—C(5)	110.8 (1)
O(1)—C(5)	1.462 (2)	N—C(2)—O(1)	108.9 (2)
C(2)—O(2)	1.193 (2)	N—C(2)—O(2)	127.0 (2)
C(4)—O(4)	1.210 (2)	O(1)—C(2)—O(2)	124.1 (2)
C(4)—C(5)	1.510 (3)	N—C(4)—O(4)	126.3 (2)
C(5)—C(7)	1.507 (3)	N—C(4)—C(5)	106.9 (2)
C(5)—C(8)	1.504 (3)	O(4)—C(4)—C(5)	127.7 (2)
Bond angles		Bond angles	
O(1)—C(5)—C(4)	102.0 (2)°	O(1)—C(5)—C(7)	108.5 (2)°
O(1)—C(5)—C(8)	109.0 (2)	C(4)—C(5)—C(7)	112.6 (2)
C(4)—C(5)—C(8)	111.4 (2)	C(7)—C(5)—C(8)	112.7 (2)

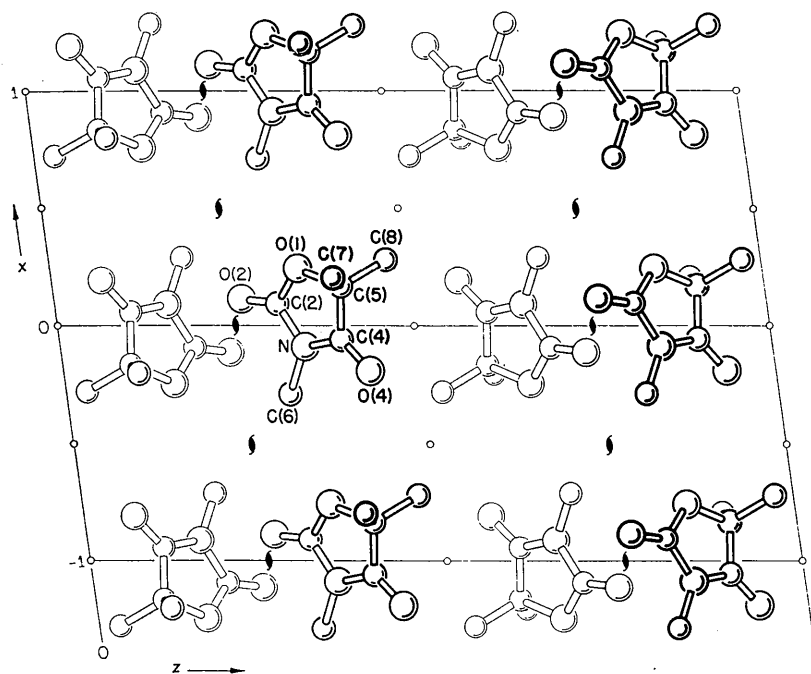


Fig. 3. A projected view down [010].

Table 8. Bond distances and angles involving the hydrogen atoms

	Distance		Distance
C(6)-C(6)H(1)	1.02 (8) Å	C(7)-C(7)H(1)	1.04 (4) Å
C(6)-C(6)H(2)	1.08 (7)	C(7)-C(7)H(2)	0.95 (3)
C(6)-C(6)H(3)	1.09 (7)	C(7)-C(7)H(3)	1.04 (3)
C(6)-C(6)H(1')	1.08 (7)	C(8)-C(8)H(1)	0.96 (3)
C(6)-C(6)H(2')	1.07 (7)	C(8)-C(8)H(2)	1.03 (3)
C(6)-C(6)H(3')	1.00 (7)	C(8)-C(8)H(3)	0.96 (4)
	Angle		Angle
C(6)H(1)-C(6)-N	107 (4)	C(7)H(1)-C(7)-C(5)	108 (2)°
C(6)H(1)-C(6)-C(6)H(2)	105 (5)	C(7)H(1)-C(7)-C(7)H(2)	112 (3)
C(6)H(1)-C(6)-C(6)H(3)	121 (5)	C(7)H(1)-C(7)-C(7)H(3)	108 (3)
C(6)H(2)-C(6)-N	108 (4)	C(7)H(2)-C(7)-C(5)	106 (2)
C(6)H(2)-C(6)-C(6)H(3)	103 (5)	C(7)H(2)-C(7)-C(7)H(3)	115 (3)
C(6)H(3)-C(6)-N	111 (3)	C(7)H(3)-C(7)-C(5)	107 (2)
C(6)H(1')-C(6)-N	108 (4)	C(8)H(1)-C(8)-C(5)	113 (2)
C(6)H(1')-C(6)-C(6)H(2')	99 (5)	C(8)H(1)-C(8)-C(8)H(2)	104 (2)
C(6)H(1')-C(6)-C(6)H(3')	111 (5)	C(8)H(1)-C(8)-C(8)H(3)	109 (3)
C(6)H(2')-C(6)-N	112 (3)	C(8)H(2)-C(8)-C(5)	108 (2)
C(6)H(2')-C(6)-C(6)H(3')	117 (6)	C(8)H(2)-C(8)-C(8)H(3)	111 (3)
C(6)H(3')-C(6)-N	108 (4)	C(8)H(3)-C(8)-C(5)	110 (2)

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