

Crystal Structures of Analogues of Purine Nucleoside. III. 2-(3'4'-Di-*O*-acetyl-2'-deoxy- β -L-erythro-pentapyranosyl)-5,6-dimethylbenzotriazole (MEBA)

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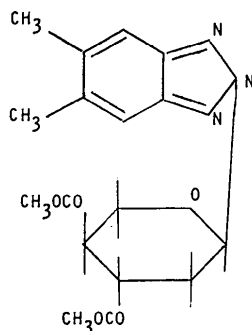
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(Received 13 February 1976; accepted 12 April 1976)

MEBA was synthesized as a potential antimetabolite. The crystal structure was determined by direct methods and refined to an R value of 7.5% by full-matrix least-squares methods. The unit cell contains two molecules and is monoclinic with $a = 11.484$ (1), $b = 7.0566$ (4), $c = 11.859$ (1) Å, $\beta = 113^\circ 36.7$ (5)'. The space group is $P2_1$. The intensities were collected on a Philips PW 1100 four-circle diffractometer. All H atoms were directly located. No unusual features with respect to the previously reported analogues have been detected.

Introduction

García-Muñoz, Iglesias, Lora-Tamayo, Madroñero & Stud (1969) have synthesized several compounds in order to investigate their activities as potential antimetabolites of purine nucleosides. The crystal structure of the first compound of this series, *cis*-ATD, has been reported by Fayos & García-Blanco (1972), and the second by López de Lerma, Martínez-Carrera & García-Blanco (1973). In the present paper we report the crystal structure of MEBA, another member of the series, based on single-crystal X-ray diffraction data collected at room temperature.



Experimental

A crystalline sample of MEBA was kindly provided by Dr García-Muñoz. The prismatic colourless crystals were mostly twinned.

A single crystal $\sim 0.3 \times 0.4 \times 0.3$ mm was selected for the X-ray investigation. The crystal belongs to the monoclinic system. The lattice constants were obtained from a least-squares analysis of the settings of 35 reflexions measured on a four-circle diffractometer with Mo $K\alpha$ radiation. The crystal data are listed in Table 1.

The ω - 2θ scan mode on the Philips PW 1100 diffractometer, monochromated with a graphite crystal,

Table 1. *Crystal data for MEBA*

Standard deviations, given in parentheses, refer to the least significant digits.

Molecular formula	$C_{17}H_{21}N_3O_5$	M.W.	347.198
Space group	$P2_1$	V	880.6 (1) Å ³
a	11.484 (1) Å	ρ_x	1.17 g cm ⁻³
b	7.0566 (4)	Z	2
c	11.859 (1)	μ	0.96 cm ⁻¹
β	$113^\circ 36.7$ (5)'	$F(000)$	368

was used for recording the intensity data. Three reflexions were monitored after every 40 measurements and showed good stability. A total of 3239 independent reflexions were collected in the range $2^\circ < \theta < 32^\circ$. Of this total 1263 were considered as unobserved according to the criterion $I < 2\sigma(I)$, where $I = C_p - C_{b_1} - C_{b_2}$ and $\sigma^2(I) = C_p + C_{b_1} + C_{b_2} + (0.04 \times I)^2$, I being the integrated intensity and $\sigma(I)$ its estimated standard deviation.

The structure amplitudes were obtained after the usual Lorentz and polarization reduction. No correction for absorption was applied because of the adequate size of the crystal used. The extinction effect did not appear to be appreciable and consequently no correction was made. The absolute scale for F_o was determined during the refinement.

Solution and refinement of the structure

17 of the 25 non-hydrogen atoms were located on an E map with the phases of 200 E 's ≥ 1.5 calculated by the multisolution tangent formula program *MULTAN* (Main, Woolfson, Declercq & Germain, 1974). The rest of the non-hydrogen atom positions were determined from a Fourier map. After six cycles of full-matrix least-squares refinement, for the 1976 observed reflexions, with isotropic temperature factors and three more cycles with anisotropic temperature factors, the conventional R value for the observed reflexions was 0.096. All hydrogen-atom positions were determined from a difference Fourier map, limiting $\sin \theta/\lambda$ to 0.5.

The refinement was continued including H atoms with fixed isotropic temperature factors equivalent to the anisotropic temperature factors of the atoms to which they are bonded (Hamilton, 1959).

An examination of the $\langle w\Delta^2 \rangle$ ($\Delta = F_o - F_c$) values as a function of $|F_o|$ and $\sin \theta$ suggested that the best weighting scheme was $w = w_1 w_2$, where $w_1 = 1/\sigma_1^2$ and $w_2 = 1/\sigma_2^2$ with $\sigma_1 = a + b|F_o|$ and $\sigma_2^2 = c + d \sin \theta/\lambda$ with the coefficients given in Table 2.

Table 2. Coefficients for weighting scheme

	a	b
$0 < F_o \leq 1.0558$	1.1962	-0.5222
$1.0558 < F_o \leq 3.963$	0.7996	-0.1039
$3.963 < F_o \leq 100.000$	0.1874	0.424
	c	d
$0 < \sin \theta/\lambda \leq 0.3400$	4.6352	-11.5395
$0.3400 < \sin \theta/\lambda \leq 0.75$	0.2183	1.1321

After least-squares refinement with these weights, the final unweighted and weighted agreement indices were $R = 0.075$ and $R_w = 0.104$, where $R_w = (\sum w\Delta^2 / \sum w|F_o|^2)^{1/2}$. A final difference synthesis had no electron density greater than $0.39 \text{ e } \text{Å}^{-3}$. The positional and thermal parameters, with estimated least-squares deviations (e.s.d.'s), are given in Tables 3 and 4.*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31849 (14 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. The positional ($\times 10^4$) and thermal ($\times 10^3$) parameters for non-hydrogen atoms

Standard deviations, given in parentheses, refer to the least significant digits. Thermal factors are those in the expression $\exp[-2\pi^2 \sum U_{ij} a_i^* a_j^* h_i h_j]$.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	7695 (3)	5748 (0)	6185 (3)	34 (1)	48 (2)	30 (1)	1 (1)	12 (1)	5 (1)
N(2)	8220 (3)	5786 (5)	5364 (2)	38 (1)	36 (1)	26 (1)	-1 (1)	10 (1)	0 (1)
N(3)	7437 (3)	5933 (6)	4177 (2)	46 (1)	41 (2)	27 (1)	-3 (2)	9 (1)	-2 (1)
C(4)	5041 (4)	6080 (7)	3276 (3)	50 (2)	38 (2)	31 (1)	1 (2)	4 (1)	-2 (2)
C(5)	4027 (4)	6063 (6)	3590 (4)	39 (2)	32 (2)	43 (2)	0 (2)	2 (1)	-7 (2)
C(6)	4183 (3)	5915 (6)	4859 (4)	36 (2)	24 (2)	52 (2)	2 (2)	12 (1)	0 (2)
C(7)	5380 (4)	5826 (7)	5779 (3)	42 (2)	41 (2)	39 (2)	2 (2)	16 (1)	-1 (2)
C(8)	6435 (3)	5855 (7)	5460 (3)	36 (1)	33 (2)	33 (2)	2 (2)	9 (1)	0 (2)
C(9)	6281 (3)	5971 (6)	4225 (3)	40 (2)	36 (2)	29 (1)	3 (2)	8 (1)	0 (1)
C(10)	2696 (4)	6196 (10)	2594 (5)	38 (2)	77 (4)	54 (3)	3 (3)	-6 (2)	-9 (3)
C(11)	3033 (4)	5840 (8)	5168 (5)	40 (2)	49 (2)	70 (3)	2 (2)	22 (2)	2 (3)
C(1')	9609 (4)	5693 (7)	5723 (3)	35 (2)	41 (2)	27 (1)	-3 (2)	15 (1)	-1 (2)
C(2')	227 (4)	4110 (7)	6645 (4)	35 (2)	42 (2)	32 (2)	4 (2)	15 (1)	2 (2)
C(3')	480 (3)	4695 (6)	7957 (3)	33 (1)	44 (2)	33 (1)	8 (1)	16 (1)	9 (1)
C(4')	1152 (3)	6602 (7)	8269 (4)	29 (2)	52 (2)	32 (2)	3 (2)	13 (1)	-6 (2)
C(5')	380 (4)	8051 (7)	7333 (4)	47 (2)	38 (2)	38 (2)	-7 (2)	16 (2)	-5 (2)
O(1')	165 (3)	7489 (5)	6097 (3)	50 (2)	39 (2)	37 (1)	-5 (1)	18 (1)	5 (1)
O(4')	2366 (3)	6419 (6)	8164 (3)	30 (1)	78 (2)	38 (1)	-4 (1)	16 (1)	-5 (2)
C(6')	3410 (5)	6723 (15)	9167 (5)	32 (2)	134 (7)	46 (3)	3 (3)	11 (2)	3 (4)
C(7')	4571 (5)	6525 (22)	8871 (7)	35 (2)	201 (12)	87 (4)	-1 (5)	26 (3)	-7 (6)
O(6')	3412 (4)	6993 (27)	112 (4)	49 (2)	449 (23)	54 (2)	8 (6)	9 (2)	-59 (7)
O(3')	1262 (3)	3242 (6)	8764 (3)	35 (1)	65 (2)	41 (1)	18 (1)	20 (1)	17 (2)
C(8')	1136 (3)	2948 (7)	9838 (4)	28 (2)	50 (2)	38 (2)	1 (2)	10 (1)	4 (2)
C(9')	2086 (5)	1543 (10)	623 (5)	43 (2)	77 (4)	54 (2)	11 (2)	18 (2)	32 (3)
O(8')	357 (9)	3743 (8)	93 (3)	62 (2)	90 (3)	47 (2)	23 (2)	34 (2)	18 (2)

Table 4. Positional ($\times 10^3$) and thermal ($\times 10^3$) parameters for hydrogen atoms

Standard deviations, given in parentheses, refer to the least significant digits. Thermal factors are $U = B/8\pi^2$.

	x	y	z	U
H(4)	504 (7)	639 (13)	252 (7)	52
H(7)	553 (7)	542 (12)	676 (7)	49
H(10a)	230 (7)	520 (12)	174 (7)	72
H(10b)	195 (8)	617 (18)	282 (7)	72
H(10c)	260 (9)	717 (16)	215 (9)	72
H(11a)	317 (9)	535 (14)	607 (8)	65
H(11b)	244 (9)	477 (15)	481 (9)	65
H(11c)	262 (9)	707 (15)	500 (8)	65
H(1')	974 (6)	524 (11)	495 (7)	44
H(2'a)	960 (7)	299 (12)	638 (7)	47
H(2'b)	104 (7)	396 (12)	656 (6)	47
H(3')	969 (6)	453 (12)	82 (6)	42
H(4')	132 (7)	709 (12)	900 (7)	47
H(5'a)	960 (7)	837 (13)	735 (7)	52
H(5'b)	78 (7)	913 (13)	745 (7)	52
H(7'a)	451 (12)	522 (23)	853 (12)	96
H(7'b)	513 (13)	667 (21)	962 (12)	96
H(7'c)	461 (12)	753 (23)	828 (12)	96
H(9'a)	287 (9)	210 (16)	138 (9)	68
H(9'b)	259 (9)	104 (16)	38 (9)	68
H(9'c)	187 (9)	48 (15)	84 (9)	68

Description of the structure and discussion

Intramolecular bond distances and angles, with their associated e.s.d.'s from the least-squares refinement, are listed in Table 5. Distances and angles are uncorrected for thermal motion. The shortest intermolecular contacts are listed in Table 6.

One can notice the abnormal, high values of some thermal (U_{22}) parameters corresponding to the C(6'),

C(7') and O(6') atoms at the end of one of the acetyl groups. This probably means that a disordered conformation exists for these atoms. The standard deviations of the positional parameters for these atoms are higher than for the remaining atoms.

The equations, in direct space, for some best least-squares planes, calculated by the method of Schomaker, Waser, Marsh & Bergman (1959), with the deviations of the atoms from these planes, are given in Table 7. The deviations of the atoms forming the dimethylbenzotriazole group and the acetyl groups show that these groups lie almost on a plane. The deviations of the atoms belonging to the pentapyranosyl ring (III) show that C(4') and C(3'), C(5') are out of the plane in opposite directions, and likewise C(1') and C(2'), O(1'). Such deviations yield a chair conformation for the pentapyranosyl ring.

In the benzene ring the distances between C(4) and C(7) (2.871), C(5) and C(8) (2.795) and C(6) and C(9) (2.761 Å) indicate that this ring is slightly elongated. A similar feature was reported in the crystal structure of *cis*-ATD (Fayos & García-Blanco, 1972) and *trans*-CLBA (López de Lerma, Martínez-Carrera & García-Blanco, 1973). The resonance structure of the benzotriazole group is indicated by some double-bond character for the C(4)–C(5), C(6)–C(7), C(9)–N(3) and C(8)–N(1) bonds. This is in good agreement with the above-mentioned crystal structures of *cis*-ATD and *trans*-CLBA.

The N–N bond lengths have values ranging from 1.46 to 1.26 Å, which correspond to the single- and double-bond distances respectively.

Table 6. Main intermolecular non-H to non-H contacts less than 3.5 Å and non-H to H contacts less than 3.0 Å

Symmetry code			
(i)	x, y, z	(v)	$2-x, \frac{1}{2}+y, 2-z$
(ii)	$1+x, y, 1+z$	(vi)	$2-x, \frac{1}{2}+y, 1-z$
(iii)	$2-x, -\frac{1}{2}+y, 2-z$	(vii)	$2-x, -\frac{1}{2}+y, 1-z$
(iv)	$1-x, \frac{1}{2}+y, 1-z$		

O(6') ^l –C(10) ^{II}	3.405 (9)	C(9') ^l —O(8') ^{III}	3.253 (7)
O(6') ^l –H(4') ^{II}	2.74 (7)	O(1') ^l —C(1') ^{VI}	3.207 (6)
O(8') ^l –H(10a) ^{II}	2.52 (11)	O(1') ^l —C(2') ^{II}	3.303 (5)
O(8') ^l –C(9') ^V	3.253 (7)	C(2') ^l —O(1') ^{III}	3.302 (5)
C(4') ^l –O(8') ^V	3.427 (7)	S(5) ^l —C(7') ^{IV}	3.452 (7)
O(8') ^l –C(8') ^V	3.443 (7)	H(11c) ^l –N(2) ^{IV}	2.77 (12)
O(8') ^l –C(4') ^{III}	3.427 (7)	H(11c) ^l –N(1) ^{IV}	2.90 (12)

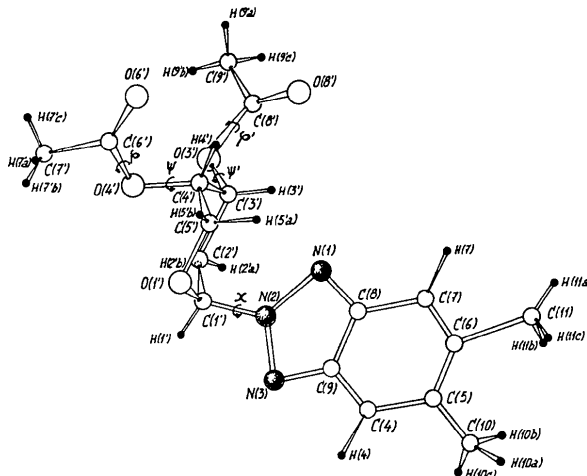


Fig. 1. Atom numbering and torsion angles.

Table 5. Intramolecular bond distances (Å) and angles (°) with their associated standard deviations given in parentheses

N(1)–N(2)	1.335 (5)	C(6')–O(6')	1.135 (9)	N(2)–N(1)–C(8)	102.4 (3)	O(1')–C(5')–C(4')	111.9 (4)
N(1)–C(8)	1.358 (4)	O(3')–C(8')	1.355 (6)	N(1)–N(2)–N(3)	117.4 (4)	C(1')–O(1')–C(5')	117.6 (3)
N(2)–N(3)	1.337 (3)	C(8')–O(8')	1.192 (7)	N(1)–N(2)–C(1')	122.6 (3)	C(4')–O(4')–C(6')	117.6 (4)
N(2)–C(1')	1.478 (5)	C(8')–C(9')	1.493 (7)	N(3)–N(2)–C(1')	120.0 (3)	O(4')–C(6')–C(7')	110.9 (5)
N(3)–C(9)	1.352 (6)	H(4)–C(4)	0.92 (9)	N(2)–N(3)–C(9)	102.4 (3)	O(4')–C(6')–O(6')	123.8 (6)
C(4)–C(5)	1.358 (7)	H(11a)–C(11)	1.07 (12)	C(5)–C(4)–C(9)	118.6 (4)	C(7')–C(6')–O(6')	126.2 (0.5)
C(4)–C(9)	1.420 (5)	H(11b)–C(11)	0.99 (11)	C(4)–C(5)–C(6)	121.6 (3)	C(3')–O(3')–C(8')	117.3 (0.4)
C(5)–C(6)	1.446 (6)	H(11c)–C(11)	0.97 (12)	C(4)–C(5)–C(10)	119.6 (4)	O(8')–C(8')–C(9')	126.1 (0.5)
C(5)–C(10)	1.515 (5)	H(10a)–C(10)	1.17 (12)	C(6)–C(5)–C(10)	118.8 (4)	O(8')–C(8')–O(3')	122.8 (0.4)
C(6)–C(7)	1.372 (5)	H(10b)–C(10)	1.00 (12)	C(5)–C(6)–C(7)	119.8 (4)	C(9')–C(8')–O(3')	111.1 (0.4)
C(6)–C(11)	1.506 (7)	H(10c)–C(10)	0.84 (13)	C(5)–C(6)–C(11)	120.0 (3)	H(4)–C(4)–C(9)	113 (5)
C(7)–C(8)	1.407 (6)	H(7)–C(7)	1.14 (8)	C(7)–C(6)–C(11)	120.1 (4)	H(11a)–C(11)–C(6)	117 (6)
C(8)–C(9)	1.405 (5)	H(1')–C(1')	1.04 (9)	C(6)–C(7)–C(8)	118.8 (4)	H(11b)–C(11)–C(6)	117 (8)
C(10)–C(5)	1.515 (5)	H(2'a)–C(2')	0.98 (7)	N(1)–C(8)–C(7)	130.0 (3)	H(11c)–C(11)–C(6)	108 (8)
C(11)–C(6)	1.506 (7)	H(2'b)–C(2')	1.03 (8)	N(1)–C(8)–C(9)	108.7 (4)	H(10a)–C(10)–C(5)	124 (6)
C(1')–C(2')	1.525 (6)	H(3')–C(3')	1.04 (8)	C(7)–C(8)–C(9)	121.3 (3)	H(10b)–C(10)–C(5)	127 (10)
C(1')–O(1')	1.409 (6)	H(4')–C(4')	0.88 (8)	N(3)–C(9)–C(4)	131.1 (4)	H(10c)–C(10)–C(5)	112 (7)
C(2')–C(3')	1.521 (6)	H(5'a)–C(5')	0.94 (9)	N(3)–C(9)–C(8)	109.1 (3)	H(1')–C(1')–C(2')	102 (4)
C(3')–C(4')	1.522 (6)	H(5'b)–C(5')	0.87 (9)	C(4)–C(9)–C(8)	119.8 (4)	H(2'a)–C(2')–C(3')	110 (5)
C(3')–O(3')	1.444 (5)	H(7'a)–C(7')	0.99 (18)	N(2)–C(1')–C(2')	112.2 (4)	H(2'b)–C(2')–C(3')	109 (4)
C(4')–C(5')	1.508 (6)	H(7'b)–C(7')	0.86 (13)	N(2)–C(1')–O(1')	110.6 (4)	H(3')–C(3')–C(4')	116 (5)
C(4')–O(4')	1.454 (6)	H(7'c)–C(7')	1.01 (19)	C(2')–C(1')–O(1')	114.3 (3)	H(5'a)–C(5')–O(1')	108 (4)
C(5')–O(1')	1.441 (6)	H(9'a)–C(9')	1.06 (10)	C(3')–C(2')–C(1')	112.2 (4)	H(5'b)–C(5')–O(1')	105 (6)
O(4')–C(6')	1.325 (5)	H(9'b)–C(9')	0.82 (13)	C(2')–C(3')–C(4')	111.1 (4)	H(7'a)–C(7')–C(6')	104 (10)
C(6')–C(7')	1.515 (10)	H(9'c)–C(9')	0.86 (13)	C(2')–C(3')–O(3')	107.4 (3)	H(7'b)–C(7')–C(6')	97 (15)
				C(4')–C(3')–O(3')	110.3 (3)	H(7'c)–C(7')–C(6')	112 (10)
				C(3')–C(4')–C(5')	109.2 (3)	H(9'a)–C(9')–C(8')	116 (17)
				C(3')–C(4')–O(4')	108.1 (4)	H(9'b)–C(9')–C(8')	120 (8)
				C(5')–C(4')–O(4')	107.3 (4)	H(9'c)–C(9')–C(8')	123 (7)

Table 7. Deviations (\AA) of atoms from some least-squares planes in the molecule, with their dihedral angles

The planes are expressed as $Ax + By + Cz = D$, where x, y and z are the fractional coordinates of the atoms.

(I) Dimethylbenzotriazole		(II) <i>O</i> -Acetyl	
$A = 0.0512$	N(1) 0.009	$A = 0.6404$	C(4') 0.006
$B = 7.0390$	N(2) -0.025	$B = 6.8883$	O(4') -0.008
$C = 0.7742$	N(3) -0.017	$C = -2.5558$	C(6') -0.001
$D = 4.5559$	C(4) -0.001	$D = 3.1375$	C(7') 0.005
	C(5) 0.001		O(6') -0.001
	C(6) 0.001		
	C(7) 0.018		
	C(8) 0.027		
	C(9) 0.010		
	C(10) 0.012		
	C(11) -0.035		

(III) Pentapyranosyl		(IV) <i>O</i> -Acetyl	
$A = 0.9963$	C(1') -0.146	$A = 6.0094$	C(3') 0.031
$B = -0.0818$	C(2') 0.171	$B = 5.0997$	O(3') -0.039
$C = -0.0268$	C(3') -0.238	$C = 2.4265$	C(8') -0.010
$D = 7.9573$	C(4') 0.263	$D = 10.5914$	C(9') 0.024
	C(5') -0.232		O(8') -0.005
	O(1') 0.181		

Dihedral angles

(I) — (II)	16.6°	(IV) — (I)	40.9°
(III) — (I)	85.5	(IV) — (II)	50.3
(III) — (II)	88.9	(IV) — (III)	63.3

Fig. 1 illustrates a molecule with all the hydrogen atoms and the torsion angles. These are $\chi = 81.0$, $\psi = 61.3$, $\phi = 2.0$, $\psi' = 30.4$ and $\phi' = 5.2^\circ$. χ is the angle between the O(1'), C(1'), N(2) and N(1), N(2), C(1') planes; ψ between the O(4'), C(4'), C(3') and C(4'), O(4'), C(6') planes; ϕ between the C(4'), O(4'), C(6') and O(4'), C(6'), C(7') planes; ψ' between the C(2'), C(3'), O(3') and C(3'), O(3'), C(8') planes; and ϕ' between the C(3'), O(3'), C(8') and O(3'), C(8'), C(9') planes. A projection of the structure along [010] is presented in Fig. 2. The packing of the molecules is entirely due to van der Waals forces.

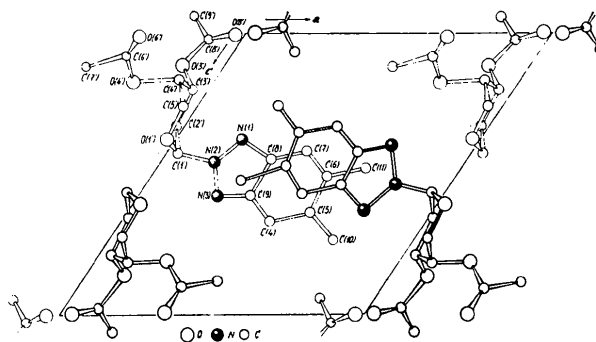


Fig. 2. A projection of the structure along [010].

The authors are grateful to Dr Garcia-Muñoz, CSIC Madrid, for generously supplying the specimens. They wish to thank the Centro de Proceso de Datos, Ministerio de Educación y Ciencia, Spain, for providing facilities for the calculation.

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