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Crystal and Molecular Structure of Diazapolycyclic Compounds. I. 2,3-Epoxy-*cis*-1,3-dimethyl-4a,9a-diaza-1,2,3,4,4a,9,9a,10-octahydroanthracene-9,10-dione

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The title compound, $C_{14}H_{14}O_3N_2$, crystallizes in the monoclinic system, $a = 5{\cdot}6735$ (4), $b = 18{\cdot}275$ (3), $c = 12{\cdot}216$ (2) Å, $\beta = 104{\cdot}58$ (1)°, $Z = 4$, $D_x = 1{\cdot}39$ g cm^{-3}, space group $P2_1/c$. The structure has been solved by direct methods and refined to $R = 0{\cdot}044$ for 1655 independent observed reflexions. The analysis shows that the epoxide ring is *trans* with respect to the C(15) methyl group. Moreover it seems that although the triangle may undergo geometrical changes its area is likely to remain constant (about 0·914 Å^2).

Introduction

A broad project on tetracycline analogues with potential pharmacological activity is under way at the Centro Nacional de Química Orgánica (CSIC Spain). One aspect of it is the synthesis of epoxide compounds which will lead, when opened, to halohydrins which can produce tetracycline analogues (Pardo Criado, 1975; Gomez Contreras, 1976) (Fig. 1). The title compound had the typical *cis–trans* uncertainty. In order to clarify this point and to obtain information about the geometry of the *N* atoms the present work was undertaken.

The crystal used in the analysis had the dimensions 0·36 × 0·36 × 0·56 mm. The crystal data are: $C_{14}H_{14}O_3N_2$, FW 257·1, monoclinic, space group $P2_1/c$, $a = 5{\cdot}6735$ (4), $b = 18{\cdot}275$ (3), $c = 12{\cdot}216$ (2) Å, $\beta = 104{\cdot}58$ (1)°, $V = 1225{\cdot}8$ Å^3, $Z = 4$, $D_x = 1{\cdot}39$ g cm^{-3}.

Intensities were collected on a Philips PW 1100 four-circle diffractometer operating in the $\omega/2\theta$ scan mode. With graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0{\cdot}71069$ Å), 2168 independent reflexions up to $\theta \leq 25°$

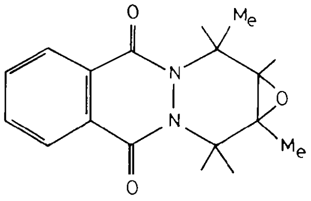

Fig. 1. Schematic formula.

Table 1. *Final positional parameters and their standard deviations, and bond distances* (Å) *for the hydrogen atoms*

	x	y	z		x	y	z	H bond
C(1)	0·6140 (3)	0·7393 (1)	0·5982 (1)	H(1)	0·785 (4)	0·743 (1)	0·621 (2)	0·94 (2)
C(2)	0·5478 (3)	0·6620 (1)	0·5648 (2)	H(2)	0·598 (4)	0·626 (1)	0·623 (2)	0·95 (2)
C(3)	0·3316 (4)	0·6473 (1)	0·4746 (2)	H(4*a*)	0·058 (5)	0·712 (2)	0·452 (2)	0·93 (3)
C(4)	0·1843 (3)	0·7106 (1)	0·4171 (2)	H(4*b*)	0·143 (4)	0·700 (1)	0·336 (2)	0·98 (2)
C(5)	0·2481 (4)	0·9581 (1)	0·2783 (2)	H(5)	0·080 (4)	0·953 (1)	0·244 (2)	0·95 (2)
C(6)	0·3907 (4)	1·0177 (1)	0·2690 (2)	H(6)	0·328 (4)	1·058 (1)	0·219 (2)	0·96 (2)
C(7)	0·6326 (4)	1·0204 (1)	0·3300 (2)	H(7)	0·730 (4)	1·061 (1)	0·321 (2)	0·95 (3)
C(8)	0·7319 (4)	0·9639 (1)	0·4003 (2)	H(8)	0·900 (5)	0·966 (1)	0·439 (2)	0·95 (2)
C(9)	0·6941 (3)	0·8464 (1)	0·4942 (2)	H(15*a*)	0·548 (4)	0·816 (1)	0·714 (2)	1·00 (3)
C(10)	0·2007 (3)	0·8345 (1)	0·3573 (1)	H(15*b*)	0·536 (4)	0·731 (1)	0·750 (2)	0·94 (2)
C(11)	0·3478 (3)	0·9007 (1)	0·3516 (1)	H(15*c*)	0·321 (5)	0·766 (1)	0·671 (2)	0·96 (3)
C(12)	0·5897 (3)	0·9041 (1)	0·4129 (1)	H(17*a*)	0·047 (5)	0·585 (2)	0·496 (3)	0·98 (3)
N(13)	0·3098 (2)	0·7815 (1)	0·4293 (1)	H(17*b*)	0·299 (6)	0·539 (2)	0·504 (3)	0·96 (3)
N(14)	0·5493 (2)	0·7875 (1)	0·4985 (1)	H(17*c*)	0·131 (5)	0·561 (1)	0·392 (2)	0·94 (3)
C(15)	0·4962 (4)	0·7649 (1)	0·6900 (2)					
O(16)	0·5727 (2)	0·6401 (1)	0·4546 (1)					
C(17)	0·1918 (4)	0·5772 (1)	0·4672 (2)					
O(18)	−0·0060 (2)	0·8262 (1)	0·2967 (1)					
O(19)	0·8982 (2)	0·8515 (1)	0·5596 (1)					

Table 2. *Bond distances* (Å), *bond angles and torsional angles* (°) *describing the geometry of the molecule*

C(1)–C(2)	1·492 (3)	C(6)–C(7)	1·388 (3)
C(1)–C(15)	1·517 (3)	C(7)–C(8)	1·371 (3)
C(1)–N(14)	1·472 (2)	C(8)–C(12)	1·389 (3)
C(2)–C(3)	1·453 (2)	C(9)–C(12)	1·468 (2)
C(2)–O(16)	1·445 (3)	C(9)–O(19)	1·234 (2)
C(3)–C(4)	1·495 (3)	C(9)–C(14)	1·363 (2)
C(3)–O(16)	1·453 (3)	C(10)–C(11)	1·468 (3)
C(3)–C(17)	1·498 (3)	C(10)–O(18)	1·231 (2)
C(4)–N(13)	1·468 (2)	C(10)–N(13)	1·361 (2)
C(5)–C(6)	1·381 (3)	C(11)–C(12)	1·390 (2)
C(5)–C(11)	1·399 (3)	N(13)–N(14)	1·413 (2)

C(15)–C(1)–C(2)	111·5 (2)	C(12)–C(9)–O(19)	122·5 (2)
C(15)–C(1)–N(14)	111·3 (2)	N(14)–C(9)–O(19)	120·8 (2)
C(2)–C(1)–N(14)	110·3 (1)	C(11)–C(10)–N(13)	116·7 (1)
C(1)–C(2)–C(3)	119·2 (2)	C(11)–C(10)–O(18)	123·3 (2)
C(1)–C(2)–O(16)	116·1 (2)	N(13)–C(10)–O(18)	119·9 (2)
C(3)–C(2)–O(16)	60·2 (1)	C(10)–C(11)–C(12)	120·5 (2)
C(2)–C(3)–C(4)	118·6 (2)	C(5)–C(11)–C(12)	119·7 (2)
C(2)–C(3)–O(16)	59·6 (1)	C(5)–C(11)–C(10)	119·7 (2)
C(2)–C(3)–C(17)	122·5 (2)	C(9)–C(12)–C(11)	120·5 (2)
O(16)–C(3)–C(17)	114·7 (2)	C(8)–C(12)–C(11)	119·9 (2)
C(4)–C(3)–O(16)	115·4 (2)	C(8)–C(12)–C(9)	119·6 (2)
C(4)–C(3)–C(17)	114·1 (2)	C(4)–N(13)–C(10)	116·4 (1)
C(3)–C(4)–N(13)	115·9 (1)	C(4)–N(13)–N(14)	119·8 (1)
C(6)–C(5)–C(11)	119·6 (2)	C(10)–N(13)–N(14)	122·9 (1)
C(5)–C(6)–C(7)	120·3 (2)	C(1)–N(14)–N(13)	116·8 (1)
C(6)–C(7)–C(8)	120·3 (2)	C(1)–N(14)–C(9)	118·5 (1)
C(7)–C(8)–C(12)	120·3 (2)	C(9)–N(14)–N(13)	122·5 (1)
C(12)–C(9)–N(14)	116·7 (1)	C(2)–O(16)–C(3)	60·2 (1)

C(1)–C(2)–C(3)–C(4)	0·8 (3)
C(2)–C(3)–C(4)–N(13)	19·6 (2)
C(3)–C(4)–N(13)–N(14)	−4·1 (2)
C(4)–N(13)–N(14)–C(1)	−32·3 (2)
N(13)–N(14)–C(1)–C(2)	50·7 (2)
N(14)–C(1)–C(2)–C(3)	−34·6 (3)
C(1)–N(14)–C(9)–C(12)	−162·6 (2)
C(1)–N(14)–C(9)–O(19)	14·2 (3)
N(13)–N(14)–C(9)–C(12)	−0·4 (2)
N(13)–N(14)–C(9)–O(19)	176·5 (2)
C(4)–N(13)–C(10)–C(11)	−167·1 (2)
C(4)–N(13)–C(10)–O(18)	9·0 (2)
N(14)–N(13)–C(10)–C(11)	1·8 (2)
N(14)–N(13)–C(10)–O(18)	177·8 (2)
C(15)–C(1)–C(2)–O(16)	158·5 (1)
H(1)–C(1)–C(2)–H(2)	61·8 (22)

were measured of which 513 were regarded as unobserved ($I < 2\sigma$). The intensities were corrected for Lorentz and polarization factors, but absorption effects were ignored. The structure was solved with the direct-method program *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1974). The set of phases (100 *E*'s) with the highest combined figure of merit revealed the positions of 13 atoms. The remaining atoms were located in a Fourier synthesis. After refinement of positional and thermal parameters by least-squares calculations, a difference synthesis revealed all the H atoms, which were included and refined in subsequent cycles (mixed mode). The data were weighted according to $w = 1/[f(F_o)]^2$ where $f(F_o) = 0{\cdot}87 - 0{\cdot}10F_o + 0{\cdot}01F_o^2$ if $F_o < 14{\cdot}5$ and $f(F_o) = 108{\cdot}25 - 11{\cdot}81F_o + 1{\cdot}07F_o^2 - 0{\cdot}02F_o^3$ otherwise. The final R and $R_w = (\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$ were 0·044 and 0·030 respectively. A final difference synthesis showed no peaks greater than 0·2 eÅ^{-3}. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974).*

Final fractional coordinates and H bond lengths are given in Table 1. Table 2 shows the geometrical features of the molecule.

Discussion

A view of the molecule defining the atomic numbering is shown in Fig. 2. Bond distances and angles have close to normal values [distances as low as 1·413 Å for a N—N bond have already been reported (Ottersen, 1973)]. The exceptions are the three C—C bonds adjacent to the epoxide ring; these bonds are significantly shorter than the usual 1·537 Å, but are in good agreement with other values given in Table 3.

The benzo and central rings are planar within 0·05 Å. O(18) and O(19) deviate from this plane by −0·14 and 0·18 Å respectively. The dihedral angle between this and the C(1)–C(2)–C(3)–C(4) plane is 31·9°. The epoxide ring makes an angle of 75·3° with the latter plane. The C(17) and C(15) substituents deviate 35 and 8° from the theoretical equatorial and axial positions, away from and towards the C(1)–C(2)–C(4)–N(13) and N(13)–N(14)–C(2)–C(3) planes respectively.

The epoxide ring is found to be *trans* with respect to the C(15) methyl group, C(15)–C(1)–C(2)–O(16) = 158·5 (1)°. The conformation of the ring to which the epoxide ring is fused is quasi 1–3 diplanar, as can be seen from torsional angles given in Table 2.

N(14) and N(13) have mean bond angles of 119·3 and 119·7° respectively (Ottersen, 1973). Following the Winkler & Dunitz (1971) criterion for amide groups, the conformational parameters are χ_N (17·7; 11·2°), χ_C(3·1; 4·0°) and τ(6·9; 5·4°) respectively.

The packing in the crystal is entirely due to van der Waals forces.

Geometrical parameters for 17 epoxide triangles are given in Table 3. They can be compared with the theoretical and experimental microwave values (*Topics in Current Chemistry*, 1973) for the oxirane molecule. CO = 1·433 − 1·436 (2), CC = 1·483 − 1·472 (2) Å,

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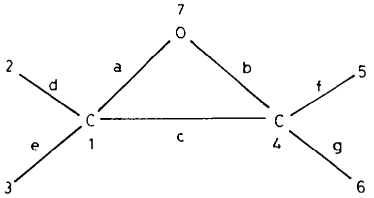
* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32772 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. *Geometry of some epoxide rings (lengths in Å, angles in degrees, area in Å²)*



Bonds	*a*	*b*	*c*	*d*	*e*	*f*	*g*	Area
1	1·449 (11)	1·445 (9)	1·465 (10)				1·487 (11)	0·915
2	1·45 (5)	1·47 (5)	1·49 (5)		1·46 (5)	1·51 (5)	1·53 (5)	0·938
3	1·437 (3)	1·458 (4)	1·465 (4)	1·495 (4)	1·488 (4)			0·914
4	1·441 (3)	1·447 (3)	1·459 (3)	1·500 (3)	1·499 (3)			0·909
	1·452 (3)	1·437 (3)	1·473 (3)		1·501 (3)		1·497 (3)	0·916
5	1·44 (1)	1·44 (1)	1·48 (1)	1·54 (1)	1·47 (1)		1·50 (1)	0·915
6	1·450 (6)	1·458 (6)	1·483 (7)		1·515 (7)	1·517 (9)	1·505 (8)	0·928
7	1·43 (4)	1·45 (4)	1·48 (4)		1·48 (4)		1·52 (4)	0·914
8	1·443 (6)	1·437 (6)	1·457 (6)		1·508 (6)		1·500 (6)	0·905
	1·439 (6)	1·429 (6)	1·463 (6)		1·509 (6)		1·501 (6)	0·903
9	1·451 (11)	1·451 (9)	1·440 (10)		1·507 (10)		1·499 (9)	0·907
10	1·442 (4)	1·438 (4)	1·450 (4)		1·504 (4)		1·498 (5)	0·903
11	1·466 (5)	1·438 (4)	1·471 (5)		1·460 (5)	1·503 (5)	1·497 (5)	0·920
12	1·445 (3)	1·453 (3)	1·453 (2)		1·492 (3)	1·498 (3)	1·495 (3)	0·911
13	1·458 (6)	1·458 (6)	1·460 (6)	1·522 (6)	1·508 (2)		1·502 (6)	0·922
14	1·419 (8)	1·451 (8)	1·485 (8)	1·481 (8)	1·514 (8)		1·520 (8)	0·912
	1·407 (8)	1·459 (8)	1·484 (8)	1·490 (8)	1·501 (8)		1·535 (8)	0·910

Angles	1	4	7	213	217	214	317	314	546	547	541	647	641
1	59·5 (4)	59·8 (4)	60·7 (4)				119·1 (4)	124·7 (5)				119·9 (6)	126·2 (6)
2	60 (2)	59 (2)	61 (2)				117 (2)	123 (2)	118 (2)	114 (2)	126 (2)	112 (2)	115 (2)
3	60·3 (2)	58·9 (2)	60·8 (2)	113·6 (2)	115·4 (2)	121·2 (3)	114·3 (2)	120·6 (3)					
4	59·9 (2)	59·4 (2)	60·7 (2)	114·6 (2)	115·2 (2)			120·6 (2)					
	58·8 (2)	59·9 (2)	61·3 (2)				115·9 (2)	122·0 (2)				116·5 (2)	119·8 (2)
5	59·3 (5)	59·0 (5)	61·7 (5)	115·1 (6)	117·0 (6)	118·8 (7)	115·3 (6)	119·7 (7)				117·0 (6)	124·6 (7)
6	59·6 (5)	59·1 (5)	61·3 (5)				114·7 (5)	126·1 (5)	116·3 (5)	114·2 (5)	123·3 (5)	115·6 (5)	115·1 (5)
7	60 (2)	58 (2)	62 (2)				121 (2)	117 (2)				115 (2)	122 (2)
8	59·4 (4)	59·8 (4)	60·8 (4)				116·9 (4)	119·3 (4)				117·0 (4)	116·1 (4)
	59·0 (4)	59·7 (4)	61·3 (4)				116·6 (4)	119·3 (4)				115·6 (4)	116·4 (4)
9	60·3 (5)	60·3 (5)	59·5 (5)				115·5 (6)	107·4 (6)				115·6 (6)	108·1 (6)
10	59·7 (2)	59·9 (2)	60·5 (2)				114·6 (3)	114·6 (3)				114·3 (3)	114·8 (3)
11	58·6 (2)	60·5 (2)	60·8 (2)				115·3 (3)	118·3 (3)	117·7 (3)	115·7 (3)	118·3 (3)	113·4 (3)	118·1 (3)
12	60·2 (1)	59·6 (1)	60·2 (1)				116·1 (2)	119·2 (2)	114·1 (2)	114·7 (2)	122·5 (2)	115·4 (2)	118·6 (2)
13	60·0 (4)	60·0 (4)	60·1 (4)	118·3 (4)	110·9 (4)	109·1 (4)	114·5 (4)	129·0 (4)				109·7 (4)	109·4 (4)
14	59·9 (4)	57·8 (4)	62·3 (4)	109·2 (4)	121·0 (4)	131·0 (4)	117·2 (4)	111·1 (4)				112·5 (4)	107·3 (4)
	60·6 (4)	57·1 (4)	62·3 (4)	109·5 (4)	119·1 (4)	130·1 (4)	119·0 (4)	112·3 (4)				111·1 (4)	105·9 (4)

References: (1) Perales & García-Blanco (1977); (2) Fayos (1976); (3) Martínez-García, Cano & García-Blanco (1977); (4) Riche (1973); (5) Pérez-Salazar, Cano, Fayos, Martínez-Carrera & García-Blanco (1977); (6) Taylor, Watson, Betkouski, Padolina & Mabry (1976); (7) Guilhem (1970); (8) Berking & Seeman (1971); (9) Saunderson, Fodor & Mandava (1971); (10) Sands (1972); (11) Ducruix, Pascard & Polonsky (1976); (12) present work; (13) Birnbaum (1973); (14) Dupont, Dideberg, Lamotte-Brasseur & Angenot (1976).

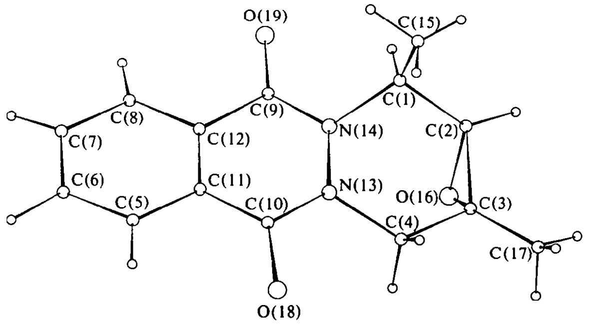


Fig. 2. A perspective view of the molecule showing the numbering system.

$C\hat{O}C$ = 62·3 – 61·6 (5), $C\hat{C}O$ = 58·8 – 59·2 (5)°, area = 0·909 – 0·907 Å².

In the following discussion the values given are $\bar{x}|S(\bar{x})|;S$, where $\bar{x}$ is the mean, $S(\bar{x})$ its error and S the dispersion of the sample:

$$\bar{x} = \frac{\Sigma(1/\sigma_i^2)x_i}{\Sigma\, 1/\sigma_i^2}; \qquad S^2(\bar{x}) = \frac{1}{\Sigma\, 1/\sigma_i^2};$$

$$S^2 = \frac{\Sigma(x-\bar{x})^2}{n-1}.$$

Two points can be established:

(*a*) The epoxide moiety seems to follow a systematic deformation so as to keep constant the area of the triangle, with variations in $C\hat{C}O$, OC′ the inverse of those in $C\hat{O}C'$, OC and CC′. For each triangle it is possible to find a maximum and a minimum value for the distances CO (Å) and for the angles $O\hat{C}C$ (°) within the epoxide ring, as follows:

$\langle CO_{max} \rangle$ = 1·451 (1);0·009
$\langle CC \rangle$ = 1·461 (1);0·014
$\langle OCC_{min} \rangle$ = 59·3 (1);0·8
$\langle CO_{min} \rangle$ = 1·439 (1);0·012
$\langle O\hat{C}C_{max} \rangle$ = 60·1 (1);0·3
$\langle$area$\rangle$ = 0·914 (2);0·009 Å^2.

(*b*) The attached substituents do not seem to differ, as far as the distances are concerned: $\langle CC \rangle$ = 1·500 (1);0·017 Å. But the angles show differences of up to $|(R\hat{C}C) - (R\hat{C}O)|$ = 11·0 (6)°; in most cases $RCC > R\hat{C}O$, but not always, and the dispersion (S) is far greater for the values in the epoxide group. Steric effects due to the rest of the substituents seem likely to be responsible for this variation, from a maximum value of 119·6 (1);4·9° to a minimum of 114·9 (1);3·4°. The angle between the substituents is fairly constant: 114·3 (1);3·2°.

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