

## The Crystal Structure of 2,6-Di-*cis*-4-hydroxyretinoic Acid $\gamma$ -Lactone\*

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$C_{20}H_{26}O_2$  is monoclinic ( $P2_1/c$ ) with  $a=11.95$  (1),  $b=10.05$  (1),  $c=15.88$  (1) Å,  $\beta=112.64$  (12)°,  $D_m=1.10$ ,  $D_c=1.12$  g cm $^{-3}$  for  $Z=4$ . The structure was solved with the Karle-Hauptmann  $\Sigma_2$  relationship and refined by full-matrix least-squares calculations. The double-bond system of the chain is in an all-*trans* configuration except for the near *cis* arrangement at the point where the chain joins the cyclohexene ring. The chain is virtually planar and is buckled near the centre. The cyclohexene ring shows some disorder and is twisted 46.3° out of the plane of the chain. The five-membered butenolide ring is planar and makes an angle of 11.3° with the plane of the chain.

### Introduction

The structure of one of the two isomeric reaction products [Fig. 1(a)] formed by the reaction of *trans*- $\beta$ -ionylidene acetaldehyde with 3-methylbut-2-enolide has already been solved (Thackeray & Gafner, 1974). The structure of the second isomer [Fig. 1(b)] which differs in the *cis* linkage at C(10) is reported here. The structures of these isomers are related to those of the vitamin A, carotene and canthaxanthin compounds.

### Experimental

Red crystals of 2,6-di-*cis*-4-hydroxyretinoic acid  $\gamma$ -lactone, provided by Dr B. V. Burger and Mr F. E. Greeff of the University of Stellenbosch, were monoclinic with space group  $P2_1/c$ , systematic absences being  $0k0$  for  $k \neq 2n$  and  $h0l$  for  $l \neq 2n$ .

A crystal with dimensions  $0.3 \times 0.5 \times 0.6$  mm was chosen. 2169 reflexions were measured by the  $\omega$ - $2\theta$  scan technique at 20°C on a Philips PW 1100 diffractometer with graphite-monochromated Mo radiation ( $\lambda=0.7107$  Å). 382 reflexions were unobserved with  $I/\sigma(I) < 1.65$ , where  $\sigma(I) = [(0.02 N_o)^2 + N_o + N_b]^{1/2}$ ,  $N_o$  is the gross and  $N_b$  the background count. Three standard reflexions measured hourly were stable to 1.5% from their mean values. Reflexions were measured from  $\theta=3$  to 22° with a scan speed of  $0.03^\circ$  s $^{-1}$  and a scan width of  $1.2^\circ$   $\theta$ . Detector apertures of  $2^\circ$  in the  $2\theta$  plane and  $1^\circ$  at right angles to it were used. The background scan time on each side was equal to half the scan time over the peak. Lorentz and polarization factors were applied but no absorption corrections were made as  $\mu R$  was only 0.02.

### Solution of the structure

As the structure of the compound was initially thought to contain a linear chain (Burger & Greeff, 1973) it was

hoped that it could be solved by Patterson methods. This approach had been successful in determining the structure of the isomeric compound 2-*cis*-4-hydroxyretinoic acid  $\gamma$ -lactone (Thackeray & Gafner, 1974) as the intermolecular vectors between the atoms in a linear chain yielded a recognizable row of vector peaks through the origin of the Patterson map. The absence of such a row implied that the chain was not linear and the structure was solved by direct methods. The phases of 175 reflexions with  $E > 1.3$  were determined and the resulting  $E$  map showed the chain atoms. A Fourier map phased on these atoms yielded the remaining non-hydrogen atom positions.

Refinement of the positional and isotropic thermal parameters reduced  $R$  to 0.163, where  $R = \sum(|F_o| - |F_c|) / \sum|F_o|$ . The function minimized was  $\sum w(|F_o| - |F_c|)^2$  and unit weights were applied. At this stage C(3), C(4), C(18) and C(19) displayed high  $B$  values of 9.87, 12.08, 7.18 and 9.47 Å $^2$ , respectively. A difference map was computed omitting these atoms. Diffuse peaks reappeared to confirm their positions.

Four cycles of anisotropic temperature refinement were executed on all the atoms reducing  $R$  to 0.104. The positions of all the hydrogen atoms were located from a difference map with the exception of one of the two attached to C(3). The hydrogen atoms were given isotropic temperature parameters equal to the overall temperature factor as determined by a Wilson plot. The remaining hydrogen atom [H(32)] could still not be located from a final difference map, and was therefore included in its calculated position.

During the final stages of refinement a weighting factor  $w$  giving less weight to those reflexions with small  $\sin \theta$  and large  $F_o$  was employed. For reflexions with  $\sin \theta < 0.35$  and/or  $F_o > 14.0$ ,  $w = \sin \theta / 0.35 \times 14.0 / F_o$ . Unit weight was assigned to the remaining reflexions. The final values of  $R$  and  $R_w$  were 0.071 and 0.084, respectively.

All calculations were carried out on an IBM 360/65 computer with the X-RAY 72 system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972). The scattering fac-

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tors for C and O used were those of Cromer & Mann (1968), and for H those of Stewart, Davidson & Simpson (1965). Table 1 lists the final atomic and thermal parameters. The labelling scheme for the atoms is given in Fig. 1(c) and bond lengths in which hydrogen atoms are involved are given in Table 2. Figs. 2 and 3 contain bond lengths and angles involving all other atoms and several least-squares planes are given in Table 3.\*

### Discussion

Apart from the near *cis* configuration of the double bonds at the point where the cyclohexene ring is attached to the chain, the double-bond system in the molecule is in an all-*trans* configuration. The chain is buckled as a result of a *cis* linkage at C(10) [Fig. 1(b)]. This accounts for our failure to locate the chain directions in the Patterson map.

Unlike the isomeric structure of 2-*cis*-4-hydroxyretinoic acid  $\gamma$ -lactone (Thackeray & Gafner, 1974), there is no apparent puckering of the cyclohexene ring as all six atoms lie approximately in the same plane (Table 3). This unexpected configuration can be attributed to disorder of C(3) and C(4) within the structure. Disorder of these atoms is a common feature of related compounds (Sly, 1964; Bart & MacGillivray, 1968; Hama-

\* The table of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30689 (15 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

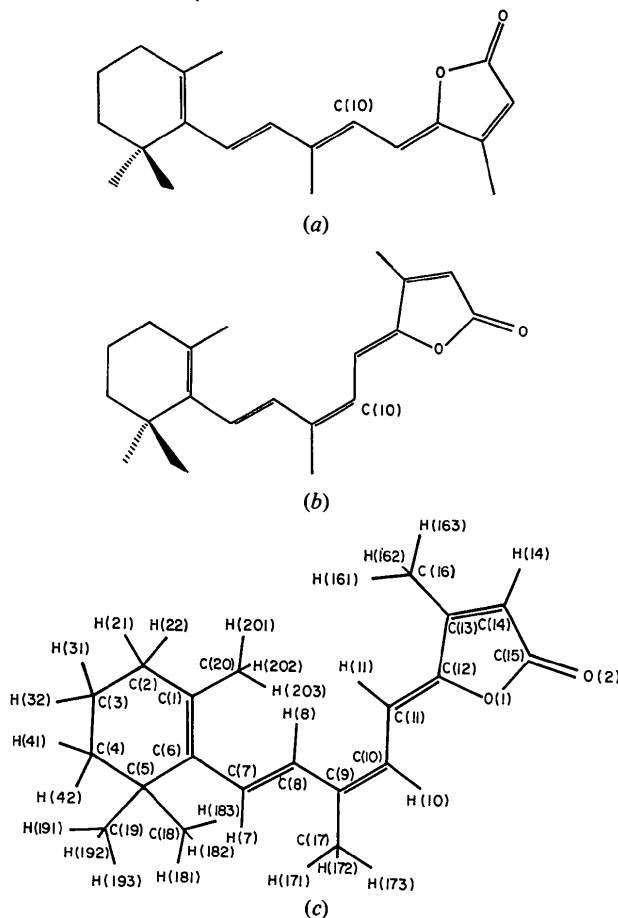


Fig. 1. (a) Conformation of the *trans*-isomer. (b) Conformation of the *cis*-isomer. (c) Labelling scheme for the atoms.

Table 1. Positional and thermal parameters

Positional parameters are given as fractional coordinates ( $\times 10^4$ ) and thermal parameters ( $\times 10^4$ ) are given according to the expression  $T = \exp[-2\pi^2(a^{*2}h^2U_{11} + b^{*2}k^2U_{22} + c^{*2}l^2U_{33} + 2a^*b^*hkU_{12} + 2a^*c^*hlU_{13} + 2b^*c^*klU_{23})]$ . Standard deviations are given in parentheses.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>11</sub>	<i>U</i> <sub>22</sub>	<i>U</i> <sub>33</sub>	<i>U</i> <sub>12</sub>	<i>U</i> <sub>13</sub>	<i>U</i> <sub>23</sub>	Isotropic <i>B</i> ( $\text{\AA}^2$ )
C(1)	6978 (4)	-1380 (3)	645 (2)	594 (27)	275 (21)	510 (26)	-5 (19)	116 (22)	4 (19)	4.08
C(2)	6379 (5)	-2084 (4)	-253 (3)	1078 (45)	434 (28)	540 (29)	-43 (29)	180 (29)	-60 (22)	5.86
C(3)	5288 (8)	-2845 (11)	-360 (6)	1189 (66)	1837 (98)	921 (55)	-508 (66)	265 (50)	-741 (64)	9.59
C(4)	4874 (12)	-2859 (14)	247 (8)	2192 (113)	2888 (144)	1311 (83)	-2254 (115)	271 (81)	-654 (90)	12.55
C(5)	5408 (4)	2232 (4)	1213 (3)	499 (26)	352 (24)	783 (32)	-95 (20)	81 (23)	59 (23)	4.52
C(6)	6534 (3)	-1418 (3)	1305 (2)	484 (24)	263 (20)	519 (25)	-24 (18)	99 (21)	48 (18)	3.49
C(7)	7095 (3)	-725 (4)	2180 (2)	457 (23)	362 (23)	454 (24)	-28 (19)	170 (19)	25 (19)	3.59
C(8)	7469 (3)	539 (3)	2329 (2)	516 (24)	331 (22)	435 (24)	-11 (19)	171 (19)	44 (18)	3.53
C(9)	7968 (3)	1182 (3)	3215 (2)	520 (24)	350 (23)	432 (23)	33 (19)	215 (20)	3 (18)	3.43
C(10)	8324 (3)	2472 (3)	3336 (2)	538 (25)	358 (23)	409 (22)	-7 (19)	179 (19)	-36 (18)	3.58
C(11)	8356 (3)	3386 (4)	2666 (2)	442 (22)	413 (22)	382 (22)	12 (18)	131 (18)	53 (18)	3.39
C(12)	8698 (3)	4674 (3)	2818 (2)	448 (21)	352 (20)	397 (21)	18 (17)	159 (17)	-32 (17)	2.89
C(13)	8890 (3)	5654 (4)	2228 (2)	458 (22)	422 (23)	497 (23)	76 (18)	171 (18)	48 (19)	3.53
C(14)	9257 (3)	6764 (4)	2714 (2)	597 (25)	343 (23)	630 (27)	-10 (20)	218 (21)	66 (21)	4.01
C(15)	9320 (3)	6539 (4)	3628 (2)	592 (26)	365 (24)	559 (27)	-13 (20)	147 (21)	-91 (21)	4.19
C(16)	8738 (4)	5388 (4)	1274 (3)	759 (31)	660 (29)	516 (25)	41 (25)	237 (23)	49 (22)	5.01
C(17)	8072 (4)	392 (4)	4037 (2)	803 (31)	577 (27)	497 (24)	-15 (24)	306 (23)	12 (20)	4.73
C(18)	5692 (5)	-3369 (5)	1871 (4)	646 (33)	737 (36)	1345 (50)	-173 (29)	251 (33)	374 (35)	7.21
C(19)	4480 (6)	-1356 (6)	1345 (8)	664 (39)	650 (39)	3398 (120)	-85 (32)	774 (56)	-23 (54)	9.41
C(20)	8125 (4)	-673 (4)	734 (3)	779 (30)	611 (28)	539 (26)	-14 (24)	324 (23)	7 (21)	4.59
O(1)	8965 (2)	5237 (2)	3671 (1)	673 (17)	366 (15)	470 (16)	-16 (13)	243 (13)	-47 (12)	3.85
O(2)	9605 (4)	7251 (3)	4286 (2)	1143 (29)	523 (19)	675 (21)	-97 (19)	258 (19)	-177 (18)	6.16
H(21)	6958 (31)	-2645 (37)	-313 (23)							3.03
H(22)	6318 (31)	-1525 (36)	-715 (23)							3.03

Table 1 (cont.)

	x	y	z	Isotropic $B(\text{\AA}^2)$
H(31)	4886 (32)	-3277 (36)	-992 (23)	3.03
H(32)	5464 (-)	-3792 (-)	-460 (-)	3.03
H(41)	4029 (34)	-2960 (38)	158 (24)	3.03
H(42)	4576 (34)	-2239 (38)	277 (24)	3.03
H(7)	7169 (32)	-1320 (36)	2732 (23)	3.03
H(8)	7419 (32)	1063 (35)	1817 (23)	3.03
H(10)	8685 (31)	2810 (36)	4026 (23)	3.03
H(11)	8140 (32)	3129 (36)	2020 (23)	3.03
H(14)	9447 (32)	7665 (36)	2530 (23)	3.03
H(161)	9372 (32)	4827 (36)	1259 (23)	3.03
H(162)	7919 (32)	5171 (36)	940 (23)	3.03
H(163)	8966 (32)	6187 (36)	971 (23)	3.03
H(171)	7230 (32)	130 (36)	3943 (23)	3.03
H(172)	8421 (32)	984 (36)	4623 (23)	3.03
H(173)	8700 (32)	-333 (36)	4113 (23)	3.03
H(181)	4976 (32)	-3855 (36)	1831 (23)	3.03
H(182)	6295 (32)	-3284 (36)	2471 (23)	3.03
H(183)	6182 (31)	-3940 (36)	1660 (23)	3.03
H(191)	4473 (32)	-423 (36)	1424 (24)	3.03
H(192)	3829 (33)	-1788 (36)	1389 (24)	3.03
H(193)	4758 (32)	-1317 (37)	1950 (24)	3.03
H(201)	7952 (31)	109 (36)	410 (23)	3.03
H(202)	8654 (31)	-400 (35)	1392 (23)	3.03
H(203)	8514 (32)	-1228 (36)	412 (23)	3.03

Table 2. Bond lengths ( $\text{\AA}$ ) involving hydrogen atoms with *e.s.d.*'s in parentheses

C(2)—H(21)	0.93 (4)	C(16)—H(163)	1.03 (4)
C(2)—H(22)	0.91 (4)	C(17)—H(171)	0.99 (4)
C(3)—H(31)	1.03 (3)	C(17)—H(172)	1.05 (3)
C(3)—H(32)	1.00 (-)*	C(17)—H(173)	1.02 (4)
C(4)—H(41)	0.97 (4)	C(18)—H(181)	0.97 (4)
C(4)—H(42)	0.73 (4)	C(18)—H(182)	0.95 (3)
C(7)—H(7)	1.04 (4)	C(18)—H(183)	0.97 (4)
C(8)—H(8)	0.95 (4)	C(19)—H(191)	0.95 (4)
C(10)—H(10)	1.07 (4)	C(19)—H(192)	0.92 (4)
C(11)—H(11)	0.99 (4)	C(19)—H(193)	0.89 (4)
C(14)—H(14)	1.00 (4)	C(20)—H(201)	0.92 (4)
C(16)—H(161)	0.95 (4)	C(20)—H(202)	1.03 (3)
C(16)—H(162)	0.94 (3)	C(20)—H(203)	0.99 (4)

\* The position of H(32) was calculated.

Table 3. Deviations of atoms from least-squares planes

(a) Deviations of the atoms from the best plane through C(6), C(7), C(8), C(9), C(10), C(11), C(12) and C(17)

C(6)	-0.028 $\text{\AA}$	C(10)	-0.024 $\text{\AA}$
C(7)	0.024	C(11)	0.036
C(8)	0.012	C(12)	-0.021
C(9)	0.004	C(17)	-0.004

(b) Deviations of the atoms from the best plane through C(1), C(2), C(3), C(4), C(5), C(6) and C(20)

C(1)	0.018	C(5)	-0.029
C(2)	0.011	C(6)	0.027
C(3)	-0.015	C(20)	-0.024
C(4)	0.013		

(c) Deviations of the atoms from the best plane through C(12), C(13), C(14), C(15), C(16), O(1) and O(2)

C(12)	-0.005	C(16)	0.022
C(13)	-0.017	O(1)	0.004
C(14)	-0.016	O(2)	0.011
C(15)	0.002		

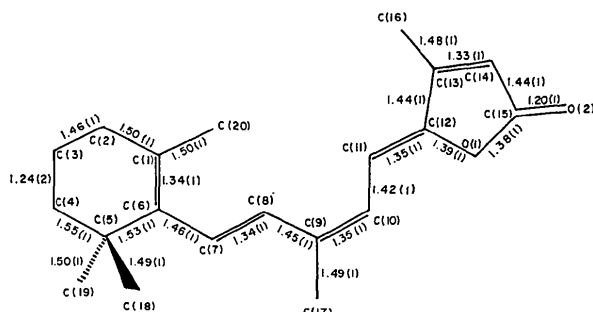


Fig. 2. Bond lengths.

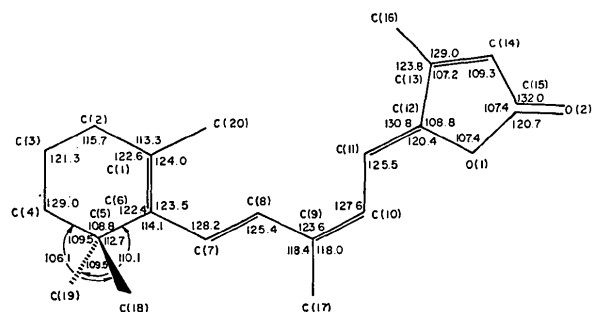


Fig. 3. Bond angles.

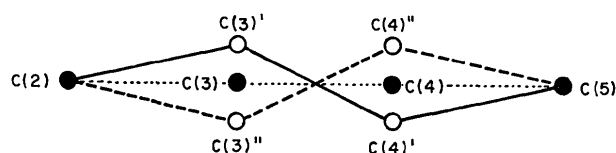


Fig. 4. A cross section of part of the cyclohexene ring. The expected conformation of the cyclohexene ring is depicted by C(2), C(3)', C(4)', C(5) or C(2), C(3)'', C(4)'', C(5). The experimentally found conformation is given by the planar group C(2), C(3), C(4), C(5) and is indicative of the disorder of C(3) and C(4).

naka, Mitsui, Ashida & Kakudo, 1972). The calculated C(3)—C(4) distance appears to be contracted to 1.24  $\text{\AA}$  as a result of this disorder. This value corresponds to the distance between C(3) and C(4) when they are situated midway between the positions they would normally occupy in the two possible puckered conformations of a cyclohexene ring (Fig. 4). It is apparent that this disorder arises from a 1:1 mixture of these two conformations in the structure.

The C(2)—C(3) distance is contracted to 1.46  $\text{\AA}$ , and this is also a result of the disorder in the cyclohexene ring. The remaining bond lengths in the ring have values close to their expected values. The chain connecting the two rings is planar within experimental error. The deviations of the atoms from the plane are given in Table 3. Mean values of 1.44 (2) and 1.35 (1)  $\text{\AA}$  for the single and double bonds in the chain are consistent with those for conjugated systems. The C—C bond angles in the chain have a mean value of 126.0°.

As in related structures the cyclohexene ring is not coplanar with the chain. The dihedral angle between the planes of the chain and the ring is 46.3° in this compound. The five-membered butenolide ring is also planar but deviates from the plane of the chain by

only 11.26°. The C-CH<sub>3</sub> bond lengths have a mean value of 1.49 (1) Å.

There is no evidence of free rotation of any methyl group. The abnormally short C(4)-H(42) bond distance of 0.73 Å arises as a result of the disorder of C(4). The remaining C-H bond distances vary between 0.89 and 1.07 Å.

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## The Crystal Structure of the 1:1 Complex between Quinol and Urea

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The complex is monoclinic, space group  $P2_1/c$ , with  $a=17.180$  (2),  $b=6.601$  (1),  $c=7.341$  (1) Å,  $\beta=94.4$  (1)°,  $Z=4$ . The structure was solved by direct methods and refined by full-matrix least-squares calculations to a final  $R$  of 0.059 for 1615 reflexions. The structure consists of alternate sheets parallel to (100) of quinol and urea molecules hydrogen-bonded together. Each oxygen atom of urea receives hydrogen bonds of lengths 2.683 (2) and 2.702 (2) Å from the OH groups of quinol molecules on either side of it in the  $x$  direction thus forming infinite chains. In addition, two of the N-H bonds of urea link to the oxygen atoms of two quinol molecules in the adjacent chain along the  $y$  direction at distances 2.980 (2) and 3.049 (3) Å and a third N-H hydrogen bonds to a quinol oxygen atom in an adjacent chain along the  $z$  direction at a distance of 3.048 (3) Å. The fourth N-H does not form a hydrogen bond.

#### Introduction

The crystal structure of the 1:1 complex between quinol, HO.C<sub>6</sub>H<sub>4</sub>.OH, and urea, CO(NH<sub>2</sub>)<sub>2</sub>, was determined as part of a series of studies of complexes formed by phenols. Each of the components is capable of forming a hydrogen-bonded framework structure which can accommodate other molecules, in cages in the case of quinol, or in channels in the case of urea. It is therefore of interest to determine the type of association which occurs when these molecules complex together.

#### Experimental

##### Crystal data

C<sub>6</sub>H<sub>6</sub>O<sub>2</sub>.CON<sub>2</sub>H<sub>4</sub>,  $M_r=170.16$ . Monoclinic,  $a=17.180$  (2),  $b=6.601$  (1),  $c=7.341$  (1) Å,  $\beta=94.4$  (1)°;  $U=830.09$  Å<sup>3</sup>,  $D_m=1.355$  (9) g cm<sup>-3</sup>,  $Z=4$ ,  $D_c=1.360$  g cm<sup>-3</sup>;  $F(000)=360$ , Mo  $K\alpha$  ( $\lambda=0.71069$  Å),  $\mu=1.16$  cm<sup>-1</sup>. Space group  $P2_1/c$  from systematic absences.

Colourless crystals of the complex were deposited when warm solutions of 1 g of quinol in 2.5 cm<sup>3</sup> of

water (to which 0.2 g of sodium sulphite were added to prevent oxidation) and 0.555 g of urea in 0.5 cm<sup>3</sup> of water were mixed and allowed to cool. Crystals more suitable for X-ray work were obtained by recrystallization from propanol. Oscillation and Weissenberg photographs established the space group and gave approximate cell dimensions. The density was determined by flotation in mixtures of chloroform and i-hibisol. A crystal of maximum dimension 0.6 mm was mounted on a Hilger and Watts, computer-controlled, four-circle diffractometer and intensities for all reflexions having  $\theta \leq 30^\circ$  were determined with Mo  $K\alpha$  radiation, a  $\theta/2\theta$  scan and a scintillation counter. Of the 2490 reflexions so measured, 1615 had net counts greater than three standard deviations of the total count and were therefore regarded as 'observed'. The intensities were corrected for Lorentz and polarization factors but not for absorption.

#### Structure determination and refinement

The solution of the structure was by direct methods. The observed and unobserved reflexions were used to obtain a scaling curve in a manner based on Wilson's