Stereochemistry of a Complex Diindenopyradione

By Judith L. Flippen-Anderson

Laboratory for the Structure of Matter, Naval Research Laboratory, Washington DC 20375, USA

AND Frank D. Mills

*Northern Regional Research Center, Agriculture Research, Science and Education Administration,
US Department of Agriculture, Peoria, Illinois 61604, USA*

Abstract

(+)-(6aSR,11aSR,11bRS)-1,6a,11a,11b-Tetrahydro-5,7,8-trimethoxy-3,6a,10,11b-tetramethyldiindeno[7,1-bc:2,1-e]pyran-2,11-dione, $C_{25}H_{26}O_6$, is triclinic and crystallizes in the space group $P\bar{1}$ with $a = 10\cdot093$ (4), $b = 13\cdot811$ (7), $c = 15\cdot916$ (6) Å, $\alpha = 77\cdot6$ (1), $\beta = 82\cdot7$ (1), $\gamma = 87\cdot5$ (1)°, $Z = 4$, $d_c = 1\cdot308$ (3) Mg m^{-3}. The X-ray study was carried out to determine the stereochemistry at the three chiral centers. The structure was solved by the symbolic addition procedure and refined on the full set of 5601 reflections to a final weighted R factor of 0·062.

Introduction

Various aminohexose-reductones (*A*), isolated from model Maillard browning reactions, have been shown to possess excellent antioxidant properties in vegetable oils and animal fats (Hodge & Evans, 1957; Evans Moser, Cooney & Hodge, 1958). Because of their inherent toxicity to laboratory animals (Ambrose, Robbins & deEds, 1961; Cutting, Furst, Read, Read & Parkman, 1960), the reductones were converted into compounds free of amines (*B*) (Mills, Hodge, Rohwedder & Tjarks, 1973), and diindenopyran (*C*) was one of the major products isolated from the mineral-acid-hydrolysis reactions (Mills, Hodge & Tjarks, 1979).

The structural assignment of *C* was based on spectral (mass spectroscopy, ^{1}H NMR, ^{13}C NMR, UV, IR) and chemical analyses. Confirmation of the structure was completed by the synthesis of *C* from 4,5-dihydroxy-3,7-dimethyl-1-indenone (Mills, 1981) and *B* (Mills *et al.*, 1979). However, the data did not allow for differentiation of the ring fusions at C(6a), C(11a) and C(11b) nor did they yield the stereochemistry of these chiral centers. The X-ray study on the per-*O*-methyl ether of *C* was performed to resolve these problems.

The methyl ether was prepared by treating *C* with potassium carbonate and methyl iodide in acetone. Colorless, rectangularly parallelepiped crystals (m.p. 483 K) were obtained by slow crystallization from absolute ethanol. The X-ray results showed that the H atom on C(11a) was *cis* with respect to the methyl on C(6a) and *gauche* to the methyl on C(11b). The numbering system used up to this point refers to that assigned by the IUPAC nomenclature rules and does not correspond to that used for the remainder of the paper. From this point on C(11a) will be referred to as C(11), C(11b) will be C(9) and C(6a) will be C(19).

Experimental

Data were collected at room temperature on a Nicolet P3F diffractometer using Cu $K\alpha$ radiation with a graphite monochromator on the incident beam. Cell dimensions were determined from a least-squares refinement on 14 independently measured reflections. The θ–2θ scan technique was used to measure the intensities of 5601 independent reflections out to a $2\theta_{max} = 112°$.

The structure was solved by application of the symbolic addition procedure for centrosymmetric crystals (Karle & Karle, 1966). The full-matrix least-squares program *ORXFLS*3 (Busing, Martin, Levy, Ellison, Hamilton, Ibers, Johnson & Thiessen, 1975) was used to refine the structure. Atomic scattering factors used were those listed in *International Tables for X-ray Crystallography* (1962). All 52 H atoms were located in difference maps calculated at various points during the anisotropic refinement.

Table 1. *Fractional coordinates and equivalent isotropic thermal parameters with e.s.d.'s in parentheses*

$$B_{eq} = \tfrac{4}{3} \sum_i \sum_j \beta_{ij}\, \mathbf{a}_i \cdot \mathbf{a}_j.$$

The IUPAC numbering scheme is given where appropriate.

		x	y	z	B_{eq} (Å²)
Molecule (I)					
O(1)	(6)	0.1963 (2)	0.8014 (2)	0.0044 (1)	4.3 (1)
C(2)	(5a)	0.3233 (3)	0.8387 (2)	−0.0163 (2)	4.0 (2)
C(3)	(5)	0.4168 (4)	0.8252 (2)	0.0424 (2)	4.1 (2)
C(4)	(4)	0.5433 (4)	0.8652 (3)	0.0149 (3)	4.5 (2)
C(5)	(3)	0.5819 (4)	0.9175 (2)	−0.0687 (2)	4.5 (2)
C(6)	(2a)	0.4849 (4)	0.9310 (2)	−0.1258 (2)	4.4 (3)
C(7)	(2)	0.4889 (4)	0.9780 (3)	−0.2188 (2)	5.3 (3)
C(8)	(1)	0.3539 (5)	0.9610 (3)	−0.2475 (3)	5.7 (3)
C(9)	(11b)	0.2635 (4)	0.9130 (3)	−0.1640 (2)	4.6 (2)
C(10)	(11c)	0.3586 (4)	0.8947 (2)	−0.0975 (2)	4.1 (2)
C(11)	(11a)	0.2015 (4)	0.8099 (3)	−0.1592 (2)	4.4 (2)
C(12)	(11)	0.2997 (4)	0.7361 (3)	−0.1949 (2)	4.6 (2)
C(13)	(10a)	0.3041 (3)	0.6444 (3)	−0.1290 (2)	4.0 (2)
C(14)	(10)	0.3765 (3)	0.5571 (3)	−0.1348 (2)	4.5 (2)
C(15)	(9)	0.3608 (4)	0.4797 (3)	−0.0629 (2)	4.8 (2)
C(16)	(8)	0.2749 (4)	0.4878 (3)	0.0108 (2)	4.6 (2)
C(17)	(7)	0.2029 (3)	0.5757 (3)	0.0158 (2)	4.4 (1)
C(18)	(6b)	0.2189 (3)	0.6539 (2)	−0.0552 (2)	4.0 (2)
C(19)	(1a)	0.1525 (3)	0.7557 (3)	−0.0635 (2)	4.4 (2)
O(20)		0.3751 (2)	0.7730 (2)	0.1234 (1)	5.3 (1)
C(21)		0.4671 (5)	0.7528 (4)	0.1858 (3)	6.4 (3)
C(22)		0.7221 (4)	0.9553 (3)	−0.0956 (3)	5.8 (2)
O(23)		0.5810 (3)	1.0223 (2)	−0.2665 (2)	6.8 (2)
O(24)		0.3586 (3)	0.7515 (2)	−0.2685 (2)	6.0 (2)
C(25)		0.4675 (5)	0.5455 (3)	−0.2146 (3)	6.0 (2)
O(26)		0.2531 (3)	0.4139 (2)	0.0827 (2)	5.6 (2)
C(27)		0.3203 (5)	0.3205 (3)	0.0811 (3)	6.0 (3)
O(28)		0.1122 (2)	0.5825 (2)	0.0873 (1)	5.0 (1)
C(29)		0.1710 (5)	0.5840 (4)	0.1642 (3)	6.2 (3)
C(30)		0.1507 (5)	0.9869 (3)	−0.1427 (3)	6.8 (3)
C(31)		0.0011 (4)	0.7520 (4)	−0.0447 (3)	5.6 (2)
Molecule (II)					
O(1A)		0.7417 (2)	0.7955 (2)	0.3997 (1)	4.2 (2)
C(2A)		0.8449 (3)	0.8183 (2)	0.4406 (2)	4.1 (2)
C(3A)		0.9710 (4)	0.8443 (2)	0.3978 (2)	4.7 (2)
C(4A)		1.0692 (5)	0.8710 (3)	0.4433 (3)	5.3 (2)
C(5A)		1.0466 (4)	0.8694 (3)	0.5317 (3)	5.2 (2)
C(6A)		0.9193 (4)	0.8421 (2)	0.5738 (2)	4.7 (2)
C(7A)		0.8601 (4)	0.8270 (3)	0.6658 (3)	5.3 (2)
C(8A)		0.7220 (5)	0.7862 (4)	0.6723 (3)	5.6 (3)
C(9A)		0.6887 (3)	0.7957 (3)	0.5786 (2)	4.5 (2)
C(10A)		0.8218 (3)	0.8208 (2)	0.5264 (2)	4.1 (2)
C(11A)		0.6443 (3)	0.7017 (3)	0.5509 (2)	4.3 (2)
C(12A)		0.7230 (3)	0.6059 (3)	0.5827 (2)	4.5 (2)
C(13A)		0.7601 (3)	0.5568 (3)	0.5097 (2)	4.3 (2)
C(14A)		0.8244 (4)	0.4655 (3)	0.5102 (2)	4.8 (2)
C(15A)		0.8556 (4)	0.4375 (3)	0.4310 (3)	5.1 (2)
C(16A)		0.8235 (4)	0.4986 (3)	0.3545 (2)	4.9 (2)
C(17A)		0.7568 (3)	0.5894 (3)	0.3553 (2)	4.5 (2)
C(18A)		0.7252 (3)	0.6179 (2)	0.4338 (2)	4.0 (2)
C(19A)		0.6563 (3)	0.7133 (3)	0.4501 (2)	4.3 (2)
O(20A)		0.9889 (2)	0.8405 (2)	0.3121 (2)	5.7 (1)
C(21A)		1.1172 (5)	0.8662 (4)	0.2645 (3)	7.8 (3)
C(22A)		1.1563 (5)	0.8954 (4)	0.5785 (4)	7.2 (3)
O(23A)		0.9121 (3)	0.8408 (2)	0.7274 (2)	7.3 (2)
O(24A)		0.7470 (3)	0.5762 (2)	0.6568 (1)	6.0 (2)
C(25A)		0.8591 (6)	0.3971 (4)	0.5913 (3)	6.7 (4)
O(26A)		0.8538 (3)	0.4760 (2)	0.2750 (2)	5.7 (2)
C(27A)		0.9362 (5)	0.3896 (4)	0.2675 (3)	6.6 (3)
O(28A)		0.7165 (2)	0.6473 (2)	0.2805 (1)	5.1 (1)
C(29A)		0.8222 (5)	0.6918 (4)	0.2176 (3)	6.8 (3)
C(30A)		0.5878 (4)	0.8821 (3)	0.5562 (3)	5.6 (2)
C(31A)		0.5214 (4)	0.7308 (4)	0.4154 (3)	5.8 (2)

Only the positional parameters for the H atoms were included in the final cycles of refinement. They were assigned *B* values equal to the final isotropic *B* values for the atoms to which they were bonded. Not all parameters could be varied in any one cycle of refinement. Consequently, only one of the molecules in the asymmetric unit was varied per refinement cycle.

Table 2. *Fractional coordinates for* H *atoms with e.s.d.'s in parentheses*

	x	y	z
Molecule (I)			
H(4)	0.606 (3)	0.857 (2)	0.055 (2)
H(8)	0.372 (3)	0.916 (3)	−0.293 (2)
H(8)	0.313 (4)	1.026 (3)	−0.279 (3)
H(11)	0.125 (4)	0.823 (3)	−0.197 (2)
H(15)	0.416 (4)	0.413 (3)	−0.064 (2)
H(21)	0.418 (4)	0.703 (3)	0.236 (3)
H(21)	0.502 (4)	0.810 (3)	0.196 (3)
H(21)	0.556 (4)	0.716 (3)	0.165 (3)
H(22)	0.777 (4)	0.924 (3)	−0.145 (3)
H(22)	0.721 (4)	1.021 (3)	−0.125 (3)
H(22)	0.777 (4)	0.942 (3)	−0.047 (3)
H(25)	0.495 (4)	0.487 (3)	−0.215 (3)
H(25)	0.539 (4)	0.587 (3)	−0.224 (3)
H(25)	0.411 (4)	0.554 (3)	−0.270 (3)
H(27)	0.422 (4)	0.330 (3)	0.071 (3)
H(27)	0.285 (4)	0.276 (3)	0.135 (3)
H(27)	0.303 (4)	0.295 (3)	0.026 (3)
H(29)	0.217 (4)	0.527 (3)	0.184 (3)
H(29)	0.100 (4)	0.592 (3)	0.209 (3)
H(29)	0.217 (4)	0.647 (3)	0.160 (3)
H(30)	0.094 (4)	0.959 (3)	−0.080 (3)
H(30)	0.185 (5)	1.047 (4)	−0.145 (3)
H(30)	0.074 (4)	0.991 (3)	−0.186 (3)
H(31)	−0.040 (4)	0.719 (3)	−0.089 (3)
H(31)	−0.026 (4)	0.717 (3)	0.022 (3)
H(31)	−0.032 (4)	0.822 (3)	−0.053 (3)
Molecule (II)			
H(4A)	1.156 (4)	0.886 (3)	0.413 (2)
H(8A)	0.657 (4)	0.824 (3)	0.705 (2)
H(8A)	0.716 (4)	0.711 (3)	0.707 (3)
H(11A)	0.529 (4)	0.686 (3)	0.572 (2)
H(15A)	0.898 (4)	0.374 (3)	0.427 (2)
H(21A)	0.102 (5)	0.852 (4)	0.209 (3)
H(21A)	0.133 (6)	0.938 (4)	0.264 (3)
H(21A)	1.191 (5)	0.828 (4)	0.295 (3)
H(22A)	1.210 (5)	0.947 (4)	0.547 (3)
H(22A)	1.214 (5)	0.844 (4)	0.594 (3)
H(22A)	1.119 (4)	0.938 (3)	0.628 (3)
H(25A)	0.791 (5)	0.377 (4)	0.626 (3)
H(25A)	0.904 (4)	0.429 (3)	0.628 (3)
H(25A)	0.905 (4)	0.337 (3)	0.583 (3)
H(27A)	1.016 (4)	0.390 (3)	0.297 (3)
H(27A)	0.884 (4)	0.324 (3)	0.302 (3)
H(27A)	0.950 (4)	0.384 (3)	0.200 (3)
H(29A)	0.796 (4)	0.747 (3)	0.178 (3)
H(29A)	0.845 (5)	0.655 (4)	0.173 (3)
H(29A)	0.904 (5)	0.708 (4)	0.237 (3)
H(30A)	0.584 (4)	0.901 (3)	0.496 (3)
H(30A)	0.610 (4)	0.949 (3)	0.583 (3)
H(30A)	0.489 (4)	0.858 (3)	0.580 (3)
H(31A)	0.545 (4)	0.735 (3)	0.350 (3)
H(31A)	0.482 (4)	0.796 (3)	0.426 (3)
H(31A)	0.452 (4)	0.670 (3)	0.448 (3)

The function minimized by the least squares was $\sum w(|F_o| - |F_c|)^2$, where the weights (w) were derived from e.s.d.'s of observed intensities (Gilardi, 1973). All reflections were included in the refinement and the final R factors were $R = 0.089$ and $R_w = 0.062$. At the end of the refinement the standard deviation for an observation of unit weight was 1·4. Table 1 lists the final positional parameters and B_{eq} values for the non-H atoms. Table 2 lists the hydrogen coordinates.*

Discussion

The results of the X-ray study are illustrated in Fig. 1. Only one molecule has been drawn since both molecules in the asymmetric unit were found to have the same conformation. The molecule consists of three essentially planar segments: the two indenone moieties [excluding methyls C(29), C(30) and C(31)], and a four-atom plane made up of C(9), C(11), C(19) and O(1). The four-atom plane bridges the two indenone systems forming a dihedral angle of 59·8 (5)° with the AB ring system and an angle of 48·2 (5)° with the $A'B'$ ring system. For molecule (II) these angles are 56·5 (5) and 43·4 (5)° respectively. Methoxy groups bonded to aromatic rings tend to be coplanar with the plane of the ring and except for C(29) the results of the present study follow this trend. C(29) is prevented from being coplanar with ring A by the H atoms on methyl C(31). The stereochemistry at the three chiral centers, C(9), C(11) and C(19) was established by this study and showed that the H atom at C(11) is *cis* with respect to C(31) and *gauche* with respect to C(30). Pertinent torsion angles are H(11)—C(11)—C(19)—C(31) at −10·6 (5)° and H(11)—C(11)—C(19)—C(30) at 51·4 (5)°. For molecule (II) these values are −15·7 (6) and 45·8 (6)°. Bond lengths and angles for the two molecules in the asymmetric unit, illustrated in Fig. 2, have expected values. There is some strain in the fused-ring system as evidenced by the long bonds to C(11). The C(11)—C(9) bond length is 1·563 (5) Å in (I) and 1·557 (5) Å in (II) and the C(11)—C(19) bond length is 1·574 (5) Å in (I) and 1·567 (5) Å in (II). The large external angles at C(6), C(13) and C(18) are common to indole moieties. The average C—H distance is 1·00 (5) Å for both molecules. The molecules form pairs around centers of symmetry as can be seen in the packing diagram in Fig. 3. There are no intermolecular contacts between molecule (II) and its symmetry-equivalent molecules that are less than van der Waals distances. The only intermolecular contacts in the cell

less than 3·5 Å are either (I)···(I) or (I)···(II) approaches, *e.g.* C(4)···C(27) at 3·41 (5), C(5)···C(27) at 3·43 (5), C(4)···C(5) at 3·44 (5) and C(12)···C(27A) at 3·48 (5) Å.
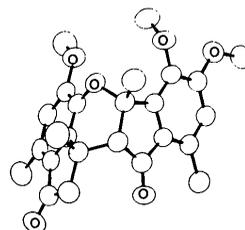

Fig. 1. *ORTEP* (Johnson, 1965) drawing of the methoxydiin-denopyradione. Atoms are shown at their final refined positions.

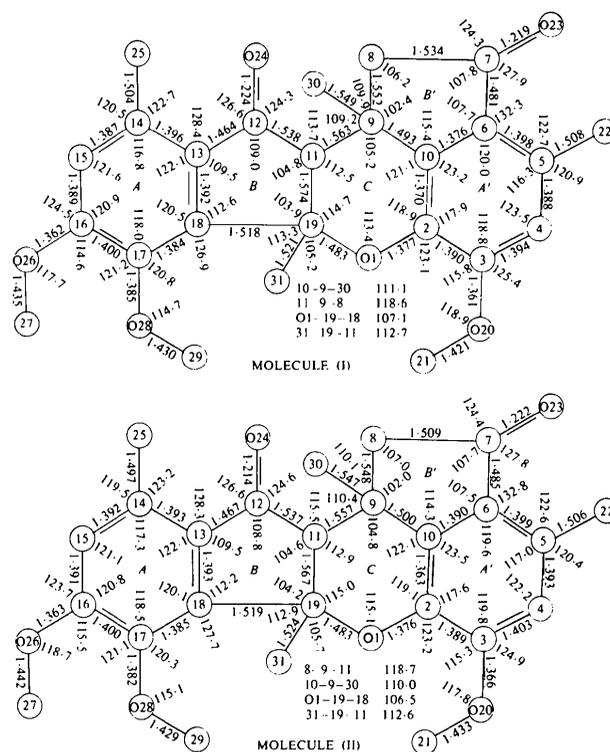Fig. 2. Bond lengths (Å) and angles (°). Standard deviations for both molecules are on the order of 0·005 Å for bond lengths and 0·3° for bond angles.

Fig. 3. Contents of one unit cell. Bonds have been blackened for both symmetry-equivalent positions for one molecule. The view is drawn with c horizontal, b approximately vertical and a coming up out of the paper.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36324 (27 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

AMBROSE, A. M., ROBBINS, D. J. & DEEDS, F. (1961). *Proc. Soc. Exp. Biol. Med.* **106**, 656–659.

BUSING, W. R., MARTIN, K. O., LEVY, H. A., ELLISON, R. D., HAMILTON, W. C., IBERS, J. A., JOHNSON, C. K. & THIESSEN, W. E. (1975). *ORXFLS3.* Oak Ridge National Laboratory, Tennessee.

CUTTING, W., FURST, A., READ, D., READ, G. & PARKMAN, H. (1960). *Proc. Soc. Exp. Biol. Med.* **104**, 381–385.

EVANS, C. D., MOSER, H. A., COONEY, P. M. & HODGE, J. E. (1958). *J. Am. Chem. Soc.* **35**, 84–88.

GILARDI, R. D. (1973). *Acta Cryst.* B**29**, 2089–2095.

HODGE, J. E. & EVANS, C. D. (1957). US Patent No. 2806794.

International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.

JOHNSON, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

KARLE, J. & KARLE, I. L. (1966). *Acta Cryst.* **21**, 849–859.

MILLS, F. D. (1981). *J. Org. Chem.* **46**, 3597–3603.

MILLS, F. D., HODGE, J. E., ROHWEDDER, W. K. & TJARKS, L. W. (1973). *J. Org. Chem.* **38**, 2512–2517.

MILLS, F. D., HODGE, J. E. & TJARKS, L. W. (1979). 178th Am. Chem. Soc. Meet. Abstr., Washington, DC. Carbohydr. Sect. No. 75.

The Structure of S,S'-Methylenebis(L-cysteine) Monohydrochloride

BY FRANCESCO BIGOLI, MAURIZIO LANFRANCHI, ENRICO LEPORATI, MARIO NARDELLI* AND MARIA ANGELA PELLINGHELLI

Istituto di Chimica Generale ed Inorganica, Università di Parma, Centro di Studio per la Strutturistica Diffrattometrica del CNR, Parma, Italy

Abstract

The crystal structure of the title compound has been determined from diffractometer data by Patterson and Fourier methods and refined to $R = 0.039$ for 1147 counter reflections: $C_7H_{15}N_2O_4S_2^+ . Cl^-$, $M_r = 290.779$, $a = 10.405$ (6), $b = 5.074$ (3), $c = 11.972$ (6) Å, $\beta = 104.9$ (1)°, $V = 610.81$ (65) Å^3, space group $P2_1$, $Z = 2$, $D_m = 1.60$, $D_c = 1.58$ Mg m^{-3}, $F(000) = 304$, $\lambda(\text{Cu } K\alpha) = 1.54178$ Å, $\mu = 6.0203$ mm^{-1}. The monovalent cation arranges the polar groups in such a way as to enclose the chloride ion. Packing is determined by a three-dimensional network of hydrogen bonds involving the protonated amino and carboxyl groups. In the very strong $O_i'' \cdots O_k''$ [2.444 (8) Å] hydrogen bond, the H atom is disordered. Other contacts involve H atoms bonded to C atoms: $C^\alpha-H \cdots O = 3.165$ (8), 3.267 (8) Å and C(methylene)–H$\cdots$O = 3.377 (9) Å. The two chemically equivalent parts of the molecule are not equivalent crystallographically and the most relevant difference between them is observed for the conformation around the $C^\beta-S^\nu$ bond, χ^2 being -169.3 (5) and -130.6 (5)°.

Introduction

As a continuation of a research programme on the conformational aspects of the sulphur-containing amino acid structures, the crystal structure analysis of S,S'-methylenebis(L-cysteine) monohydrochloride (djenkolic acid monohydrochloride),

$$^-OOC-\underset{\underset{NH_3^+}{|}}{CH}-CH_2-S-CH_2-S-CH_2-\underset{\underset{NH_3^+}{|}}{CH}-COO^- . HCl$$
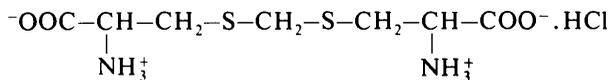
has been carried out. The present study is connected with previous work on crystals of DL-homocystine itself and of its monohydrogen oxalate (Bigoli, Lanfranchi, Leporati, Nardelli & Pellinghelli, 1981).

Experimental

Attempts to obtain single crystals of L-djenkolic hydrochloride from aqueous solutions were unsuccessful, while clear, colourless needle-like single crystals of the title compound were obtained when attempting to prepare a copper(I) complex, *i.e.* by adding commercial L-djenkolic acid to a saturated solution of CuCl in 37% hydrochloric acid. From these